

# Bedside Medicine

**Without Tears**

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**SN Chugh**

**Bedside  
Medicine**

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**BEDSIDE MEDICINE**  
**WITHOUT TEARS**

# BEDSIDE MEDICINE WITHOUT TEARS

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### **Bedside Medicine Without Tears**

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*Dedicated to  
My parents  
Late Shri Chhabil Dass Chugh and Sanwari Devi  
and my wife Dr Kiran Chugh  
and  
My children  
Daughter Dr Ashima Chugh  
Son Dr Anshul Chugh  
Daughter-in-law Dr Deepti Chugh  
and my teachers and students*

# Preface

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I have realised over the years that the students are not oriented well to practical examinations and face difficulty in the interpretation of clinical signs. They lack basic sense to analyse the symptoms and signs probably because either they do not attend the clinical classes or they lay more stress on theoretical discussion. In clinical case discussion, the questions are asked according to the interpretation of clinical symptoms and signs, and the students find difficulty in answering them because they are not ready to face practical examination immediately after the theory examination. The students prepare the subject for theory paper from the Textbook of Medicine but they do not have too many books on practical aspects of medicine. After the theory papers, the time given to the students is short to prepare for practical examination. They want to revise the subject as a whole for practical examinations because the examiners in practical examination do not limit themselves only to practical aspects but also can forward questions on theoretical aspects of medicine.

Today, the students want such a book which can orient them not only to clinical examination but also prepare them to face theoretical discussion about the case. Keeping in view the dire necessity of a book which can cater the needs of the students to their satisfaction and allow them to face the examination “without tears in their eyes”, I am bringing out the first edition of this book after consultations with students, residents and my teacher colleagues. I hope this book will not disappoint them at the hour of need.

The medicine being an ever-changing science, it is difficult to cope with the recent advances. I have attempted to include all the available informations in the literature, so as to present this book as updated. However, “to err is human”, and I am conscious of my deficiencies, therefore, I may be excused for any lapse or deficiency in this book as this is written by a single author.

I extend my sincere thanks to M/s Jaypee Brothers Medical Publishers (P) Ltd., for bringing the excellent first edition of the book. The publisher has taken special care to depict the clinical material provided to him clearly and carefully for which I am highly indebted. My special thanks to Mr Atul Jain of Jain Book Depot, Rohtak who had played vital role in the preparation of this book.

Mere words are not sufficient to express appreciation for my wife and children who have supported me during this period. I can say that it was impossible for me to bring out this book without their moral support.

At last, I request the readers to convey their suggestions or comments regarding this book to the publisher or author.

**SN Chugh**

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# 1

# Clinical Case Discussion

## LONG CASES

### CASE 1: CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) WITH OR WITHOUT COR PULMONALE

The patient (Fig. 1.1A) presented with cough with mucoid sputum for the last 8 years. These symptoms intermittently increased during windy or dusty weather. No history of hemoptysis, fever, pain chest. The sputum is white, small in amount with no postural relation.

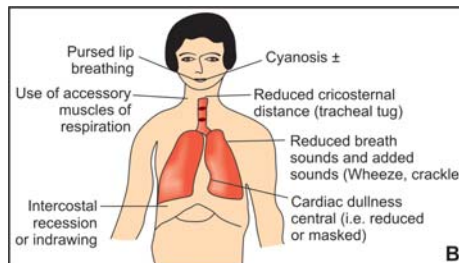
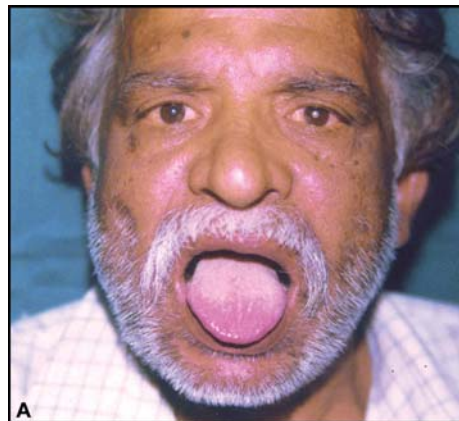
#### Points to be Stressed in History

- **Cigarette smoking.** Exposure to smoke from cigarette or biomass and solid fuel fires, atmospheric smoke is important factor in pathogenesis as well as in acute exacerbation of COPD. The smoke has adverse effect on surfactants and lung defence.
- **Precipitating factors,** e.g. dusty atmosphere, air pollution and repeated upper respiratory tract infections. They cause acute exacerbations of the disease.
- **Family history:** There is increased susceptibility to develop COPD in family of smokers than non-smokers.
- **Hereditary predisposition.** Alpha-1-antitrypsin deficiency can cause emphysema in non-smokers adult patients.

#### Physical Signs (See Table 1.1)

##### General Physical

- Flexed posture (leaning forward) with pursed-lip breathing and arms supported on their knees or table.



**Figs 1.1A and B:** Chronic obstructive pulmonary disease (COPD): A. Patient of COPD demonstrating central cyanosis. B. Clinical signs of COPD (Diag)

#### Clinical Presentations

- Initially, the patients complain of repeated attacks of productive cough, usually after colds and especially during winter months which show a steady

#### Examination

##### Inspection

##### Shape of the chest

- AP diameter is increased relative to transverse diameter.
- **Barrel-shaped chest:** the sternum becomes more arched, spines become unduly concave, the AP diameter is > transverse diameter, ribs are less oblique (more or less horizontal), subcostal angle is wide (may be obtuse), intercostal spaces are widened.

##### Movements of the chest wall

- Bilaterally diminished

##### Respiratory rate and type of breathing

- Pursed-lip breathing
- Intercostal recession (indrawing of the ribs)
- Excavation of suprasternal, supra-clavicular and infraclavicular fossae during expiration
- Widening of subcostal angle
- Respiratory rate is increased. It is mainly abdominal. The alae nasi and extra-respiratory muscles are in action.

All these signs indicate hyperinflation of lung due to advanced airflow obstruction.

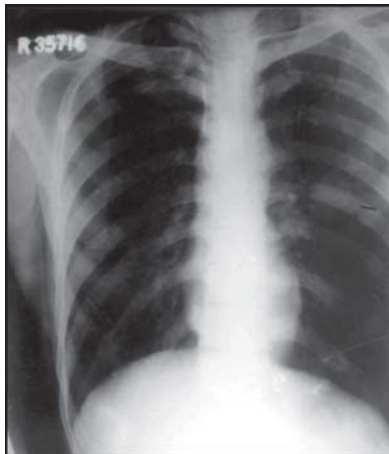
- Cardiac apex beat may or may not be visible.

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- Central cyanosis, may be noticed in severe COPD.
- Bounding pulses (wide pulse pressure) and flapping tremors on outstretched hands may be present in severe COPD with type 2 respiratory failure. These signs suggest hypercapnia.
- Disturbed consciousness with apnoeic spells ( $\text{CO}_2$  narcosis-type 2 respiratory failure).
- Raised JVP and pitting oedema feet may be present if patient develops cor pulmonale with congestive heart failure.

Oedema feet without raised JVP indicate secondary renal amyloidosis due to pulmonary suppuration, e.g. bronchiectasis, bronchitis, chest infections.

- Respiratory rate is increased (hyperpnoea). There may be tachycardia.



**Fig. 1.1:** Chest-X-ray PA view showing hyperinflated (hyper-translucent) lungs and tubular heart

increase in severity and duration with successive years until cough is present throughout the year for more than 2 years.

- Later on with increase in severity of the disease, patient may complain of repeated chest infections, exertional breathlessness, regular morning cough, wheeze and occasionally chest tightness.
- Patient may present with acute exacerbations in which he/she develops fever, productive cough, thick mucopurulent or purulent sputum, often streaked with blood (haemoptysis) and increased or worsening breathlessness.
- Patient may present with complications, the commonest being *cor pulmonale*, characterised by right ventricular hypertrophy with or without failure. The symptoms of right ventricular failure include, pain in right hypochondrium, ascites (swelling of abdomen) and swelling of legs (oedema).

### Palpation

- Movements of the chest are diminished bilaterally and expansion of the chest is reduced.
- Trachea is central but there may be reduction in length of palpable trachea above the sternal notch and there may be tracheal descent during inspiration (tracheal tug).
- Intercostal spaces may be widened bilaterally.
- Occasionally, there may be palpable wheeze (rhonchi) during acute exacerbation.
- Cardiac apex beat may not be palpable due to superimposition by the hyperinflated lungs.

### Percussion

- A hyper-resonant note on both sides.
- Cardiac dullness is either reduced or totally masked
- Liver dullness is pushed down (below 5th intercostal space).
- There may be resonance over **Kronig's isthmus** and **Traube's area** (splenic dullness is masked).
- Diaphragmatic excursions are reduced.
- Tactile vocal fremitus may be reduced bilaterally. It can be normal in early cases.

### Auscultation

- Breath sounds may be diminished in intensity due to diminished air entry.
- Vesicular breathing with prolonged expiration is a characteristic sign of COPD.
- Vocal resonance may be normal or slightly diminished on both sides equally.
- Rhonchi or wheeze are common especially during forced expiration (expiratory wheeze/rhonchi). Sometimes crackles may be heard during acute exacerbation of chronic bronchitis.

## Common Questions and Their Appropriate Answers

### 1. What is COPD?

**Ans.** Chronic obstructive pulmonary disease is the internationally recognised term, includes chronic bronchitis and emphysema.

By definition, COPD is a chronic progressive disorder characterised by airflow obstruction ( $FEV_1 < 80\%$  predicted and  $FEV_1/FVC$  ratio  $< 70\%$ ) which does not change markedly over several months.

### 2. How do you define chronic bronchitis?

**Ans.** Chronic bronchitis is a condition characterised by cough with or without expectoration on most of the days in a week for at least 3 months in a year for 2 consecutive years (WHO). Chronic bronchitis simply denotes mucoid sputum production. Chronic bronchitis with acute exacerbation means, fever, persistent or recurrent mucopurulent sputum in the absence of localised suppurative lung disease, e.g. bronchiectasis.

### 3. How COPD differs from bronchial asthma?

**Ans.** The differences between COPD and bronchial asthma are given in Table 1.2.

### 4. How do you classify severity of COPD?

**Ans.** Severity of COPD is discussed in Table 1.3.

### 5. How do you decide about which component of COPD is predominant, i.e. chronic bronchitis or emphysema?

**Ans.** Though COPD encompasses both chronic bronchitis and emphysema but one may predominate over the other. Clinically, patients with predominant bronchitis are referred as “blue-bloaters” (blue refers to cyanosis, bloater-oedema) and with predominant emphysema as pink puffers (pink refers to absence of cyanosis, puffers-pursed-lip breathing). The difference between the two is enlisted in Table 1.4.

### 6. What are the signs of advanced airflow obstruction?

**Ans.** Main signs are as follows:

- Dyspnoea and even orthopnoea with purse-lip breathing (a physiologic response to decreased air entry).
- Excavation of the suprasternal notch, supraclavicular fossae during inspiration, together with indrawing (recession) of intercostal spaces.
- Barrel-shaped chest (AP diameter  $\geq$  transverse diameter) with horizontality of the ribs.
- A reduction in the length of trachea palpable above the suprasternal notch.
- Contractions of extra-respiratory (accessory) muscles (sternomastoid and scalene muscles) on inspiration
- Central cyanosis
- Expiratory filling of neck veins
- Flapping tremors and bounding pulses (due to hypercapnia)
- Wheeze (rhonchi) especially on forced expiration.

### 7. What do you understand by the term emphysema? What are its bed side diagnostic signs?

**Ans.** Emphysema is defined as hyperinflation or overdistension of air spaces (e.g. alveoli) distal to terminal bronchioles as well as destruction of the alveolar septae.

*Bedside diagnostic signs are:*

- Pursed-lip breathing
- Barrel-shaped chest
- Apex beat is not visible
- Diminished movements of chest with reduced expansion
- Diminished vocal fremitus and vocal resonance
- Hyper-resonant percussion note on both sides
- Cardiac and liver dullness masked
- Heart sounds may get muffled
- Usually wheeze or crackles are absent
- Liver may become palpable due to descent of diaphragm.

### 8. What are complications of COPD?

**Ans.** Common complications are as follows:

- *Pneumothorax* due to rupture of bullae into pleural space
- *Recurrent pulmonary infections*
- *Cor pulmonale* (right ventricular hypertrophy with pulmonary arterial hypertension)
- *Congestive cardiac failure* (raised JVP, hepatomegaly, cyanosis, ascites, peripheral oedema with RVH).



Table 1.1: Important differential physical signs in various respiratory disorders

Sign	Lobar consolidation	Lobar collapse	Fibrosis/ bronchiectasis	Cavity or lung abscess	Pleural effusion	Pneumo-thorax	Acute or chronic bronchitis	Bronchial asthma	Emphy-sema
1. Shape of the chest	N	Retraction on the side involved	Retraction on the side involved	N or slight retraction on the side involved	N	N	N	N	Hyper-inflated or barrel shaped
2. Chest wall movement	Reduced on the side involved	Reduced on the side involved	Reduced on the side involved	Slightly reduced on the side involved	Reduced or absent on the side involved	Reduced or absent on the side involved	N	Bilateral diminished	Bilateral diminished
3. Expansion of chest	Reduced on the side involved	Reduced on the side involved	Reduced on the side involved	Slightly reduced on the side involved	Reduced or absent on the side involved	Reduced or absent on the side involved	N	B/L reduced	B/L reduced
4. Activity of extrathoracic muscles	A	A	A	A	A	A	P	P	P
5. Position of trachea and mediastinum	N	Shifted to the side involved	Shifted to the side involved	Shifted to the side involved	Shifted to opposite side	Shifted to opposite side	N	N	N
6. AP and transverse diameter	N	N	N	N	N	N	N or abnormal	N	Abnormal AP > T
7. Vocal fremitus	Increased on the side involved	Reduced or absent on the side involved	Increased over the area involved	Increased over the area involved	Reduced or absent on the side involved	Reduced or absent on the side involved	N	N	N or reduced on both sides
8. Percussion note	Dull on the side involved	Dull on the side involved	Impaired over the area involved	Impaired over the area involved	Stony dull on the side involved	N or hyper-resonant on the side involved	N	N or hyper-resonant during acute attack	Hyper-resonant
9. Breath sounds	High-pitched bronchial over the area involved	Diminished or absent over the area involved	Low-pitched bronchial over the area involved	Amphoric bronchial over the area involved	Absent or diminished over the area involved	Absent or diminished on the side involved	B/L vesicular with prolonged expiration	B/L vesicular with prolonged expiration	B/L vesicular with prolonged expiration
10. Intensity of breath sounds (vocal resonance)	Increased over the area involved. Bronchophony and whispering pectoriloquy present	Decreased over the area involved	Increased over the area involved	Increased over the area involved whispering pectoriloquy present	Decreased over the area involved	Decreased on the side involved	N	N	N or diminished
11. Added sounds	Fine crepitations early coarse crepitations later on the area involved	None	Coarse crepitations on the area involved	Coarse crepitations on the area involved	Pleural rub in some cases over the area involved	None	Rhonchi with some coarse crepitations on both the sides	Rhonchi, mainly expiratory and high-pitched	Expiratory rhonchi

Abbreviation: N = normal; B/L = bilateral; P = present; A = absent; AP = antero-posterior

**Table 1.2:** Differentiating features between bronchial asthma and COPD

<i>Bronchial asthma</i>	<i>COPD (Fig. 1.1B)</i>
<ul style="list-style-type: none"> <li>Occurs in young age, seen in children and adults who are atopic</li> <li>Allergo-inflammatory disorder, characterised by reversible airflow obstruction, airway inflammation and bronchial hypersensitivity.</li> <li>Short duration of symptoms (weeks or months)</li> <li>Episodic disease with recurrent attacks</li> <li>Variable nature of symptoms is a characteristic feature</li> <li>Family history of asthma, hay fever or eczema may be positive</li> <li>A broad dynamic syndrome rather than static disease</li> <li>Wheezing is more pronounced than cough</li> <li>Shape of the chest remains normal because of dynamic airway obstruction but AP diameter may increase with severe asthma</li> <li>Pursed-lip breathing is uncommon</li> <li>Respiratory movement may be normal or decreased, tracheal tug absent. Accessory muscles of respiration may be active and intercostal recession may be present.</li> </ul>	<p>Occurs in middle or old aged persons</p> <p>Inflammatory disorder characterised by progressive airway obstruction</p> <p>Long duration of symptoms, e.g. at least 2 years</p> <p>Nonepisodic usually but acute exacerbations may occur which worsen the symptoms and disease further</p> <p>Symptoms are fixed and persistent, may be progressive</p> <p>No positive family history</p> <p>A chronic progressive disorder</p> <p>Cough is more pronounced and wheezing may or may not be present</p> <p>Barrel-shaped chest (AP diameter <math>\geq</math> transverse) in patients with predominant emphysema</p> <p>Pursed-lip breathing common</p> <p>Respiratory movement are usually decreased with:</p> <ul style="list-style-type: none"> <li>Reduced palpable length of trachea with tracheal tug</li> <li>Reduced expansion</li> <li>Excavation of suprasternal notch, supraclavicular and infraclavicular fossae.</li> <li>Widening of subcostal angle</li> <li>Intercostal recession</li> <li>Accessory muscles of respiration hyperactive.</li> </ul>

**Table 1.3:** Gold criteria for severity of COPD

<i>Gold stage</i>	<i>Severity</i>	<i>Symptoms</i>	<i>Spirometry</i>
0	At risk	Chronic cough, sputum	Normal
I	Mild	With or without chronic cough or sputum production	FEV <sub>1</sub> /FVC < 70% FEV <sub>1</sub> = 80% predicted
II	Moderate	With or without chronic cough or sputum production	FEV <sub>1</sub> /FVC < 70% FEV <sub>1</sub> = 50 to 80% predicted
III	Severe	-do-	FEV <sub>1</sub> /FVC < 70% FEV <sub>1</sub> = 30-50%
IV	Very severe	-do-	FEV <sub>1</sub> /FVC < 70% FEV <sub>1</sub> < 30%
			Or FEV <sub>1</sub> < 50% predicted with respiratory failure or signs of right heart failure

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**Table 1.4:** Differences between chronic bronchitis and emphysema

Features	Predominant chronic bronchitis (blue bloaters)	Predominant emphysema pink puffers)
Age at the time of diagnosis (years)	60 ±	50 ±
Major symptoms	Cough > dyspnoea, cough starts before dyspnoea	Dyspnoea > cough; cough starts after dyspnoea
Sputum	Copious, purulent	Scanty and mucoid
Episodes of respiratory infection	Frequent	Infrequent
Episodes of respiratory insufficiency	Frequent	Occurs terminally
Wheeze and rhonchi	Common	Uncommon
Chest X-ray	Enlarged cardiac shadow with increased bronchovascular markings	Increased translucency of lungs (hyperinflation), central tubular heart, low flat diaphragm
Compliance of lung	Normal	Decreased
Airway resistance	High	Normal or slightly increased
Diffusing capacity	Normal to slight decrease	Decreased
Arterial blood gas	Abnormal in the beginning	Normal until late
Chronic cor pulmonale	Common	Rare except terminally
Cardiac failure	Common	Rare except terminally

- *Type 2 respiratory failure* (CO<sub>2</sub> narcosis) with flapping tremors, bounding pulses, worsening hypoxia and hypercapnia
- *Secondary polycythemia* due to hypoxia.

### Clinical tips

1. A sudden worsening of dyspnoea after prolonged coughing indicate pneumothorax due to rupture of bullae.
2. Oedema of the legs in COPD indicates CHF
3. Flaps on outstretched hands indicate type 2 respiratory failure.

### 9. How will you investigate the patient?

**Ans.** The following investigations are usually performed;

1. Haemoglobin, TLC, DLC and PCV for anaemia or polycythemia (PCV is increased) and for evidence of infection.
2. *Sputum examination.* It is unnecessary in case of COPD but during acute exacerbation, the organisms (*Strep. pneumoniae* or *H. influenzae*) may be cultured). Sensitivity to be done if organisms cultured.
3. Chest X-ray (See Fig. 1.1C) will show;

- Increased translucency with large voluminous lungs
- Prominent bronchovascular markings at the hilum with sudden pruning/ truncation in peripheral fields
- Bullae formation
- Low flat diaphragm. Sometimes, the diaphragm shows undulations due to irregular pressure of bullae
- Heart is tubular and centrally located.

**Tip.** An enlarged cardiac shadow with all of the above radiological findings suggests cor pulmonale.

4. *Electrocardiogram (ECG).* It may show;
  - Low voltage graph due to hyperinflated lungs
  - P-pulmonale may be present due to right atrial hypertrophy.
  - Clockwise rotation of heart
  - Right ventricular hypertrophy (R>S in V<sub>1</sub>)
5. *Pulmonary function tests.* These show **obstructive ventilatory defect** (e.g. FEV<sub>1</sub>, FEV<sub>1</sub>/VC and PEF-all are reduced, **lung volumes** – total lung capacity and residual volume increased and **transfer factor CO** is reduced). The difference between obstructive

**Table 1.5:** Pulmonary function tests in obstructive and restrictive lung defect

Test	Obstructive defect (COPD)	Restrictive defect (Interstitial lung disease)
Forced expiratory volume during one second (FEV <sub>1</sub> )	Markedly reduced	Slightly reduced
Vital capacity (VC)	Reduced or normal	Markedly reduced
FEV <sub>1</sub> /VC	Reduced	Increased or normal
Functional residual capacity (FRC)	Increased	Reduced
Peak expiratory flow (PEF)	Reduced	Normal
Residual volume (RV)	Increased	Reduced
Total lung capacity	Increased	Reduced
Transfer or diffusion factor for CO (T <sub>co</sub> and D <sub>co</sub> )	Normal	Low
PaO <sub>2</sub>	Decreased	Decreased
PaCO <sub>2</sub>	Increased	Low or normal

and restrictive lung defect are summarised in Table 1.5.

6. *Arterial blood gas analysis* may show reduced PaO<sub>2</sub> and increased PaCO<sub>2</sub> (hypercapnia).
7. *Alpha-1 antitrypsin levels*: Reduced level may occur in emphysema (normal range is 24 to 48 mmol/L).

### 10. What do you understand by the term chronic Cor pulmonale?

**Ans.** *Chronic Cor pulmonale* is defined as right ventricular hypertrophy/dilatation secondary to chronic disease of the lung parenchyma, vascular and/or bony cage. Therefore its causes include;

#### I. Diseases of the lung (hypoxic vasoconstriction)

- COPD
- Diffuse interstitial lung disease
- Pneumoconiosis (occupational lung disease).

#### II. Diseases of pulmonary vasculature

- Primary pulmonary hypertension
- Recurrent pulmonary embolism
- Polyarteritis nodosa

### III. Disorders of thoracic cage affecting lung functions

- Severe kyphoscoliosis
- Ankylosing spondylitis
- Neuromuscular disease, e.g. poliomyelitis
- Obesity with hypoventilation (*Pickwickian syndrome*)

**Acute Cor pulmonale** refers to acute thromboembolism where pulmonary hypertension develops due to increased vascular resistance leading to right ventricular dilatation with or without right ventricular failure.

### 11. Are cor pulmonale and right heart failure synonymous?

**Ans.** No, cor pulmonale just refers to right ventricular hypertrophy and dilatation. Right ventricular failure is a step further of hypertrophy or dilatation, hence, is considered as a complication of Cor pulmonale.

### 12. What do you understand by term obstructive sleep-apnoea syndrome?

**Ans.** Obstructive sleep-apnoea syndrome is characterised by spells of apnoeas with snoring due to occlusion of upper airway at the level of oropharynx during sleep.

Apnoeas occur when airway at the back of throat is sucked closed during sleep. When awake, this tendency is overcome by the action of the muscles meant for opening the oropharynx which become hypotonic during sleep. Partial narrowing results in snoring, complete occlusion in apnoea and critical narrowing in hyperventilation. The major features include, loud snoring, day-time somnolence, unfreshed or restless sleep, morning headache, nocturnal choking, reduced libido and poor performance at work, morning drunkenness and ankle oedema. The patient's family report the pattern of sleep as "snore-silence-snore" cycle. The diagnosis is made if there are more than 15 apnoeas/hyperpnoeas in any one hour of sleep with fall in arterial O<sub>2</sub> saturation on ear or finger oximetry.

### 13. What is congenital lobar emphysema?

**Ans.** Infants rarely develop a check-valve mechanism in a lobar bronchus, which leads to rapid and life-threatening unilateral overdistension of alveoli, called *congenital lobar emphysema*.

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### 14. What is unilateral emphysema? What are its causes?

**Ans.** Overdistension of one lung is called *unilateral emphysema*. It can be congenital or acquired (compensatory emphysema). Unilateral compensatory emphysema develops due to collapse or destruction of the whole lung or removal of one lung.

*Macleod's or Swyer-James syndrome* is characterised by unilateral emphysema developing before the age of 8 years when the alveoli are increasing in number. This is an incidental radiological finding but is clinically important because such a lung is predisposed to repeated infections. In this condition, neither there is any

obstruction nor there is destruction and overdistension of alveoli, hence, the term emphysema is not true to this condition. In this condition, the number of alveoli are reduced which appear as larger airspaces with increased translucency on X-ray.

### 15. What do you understand by the term bullous emphysema?

**Ans.** Confluent air spaces with dimension  $> 1$  cm are called *bullae*, may occasionally be congenital but when occur in association with generalised emphysema or progressive fibrotic process, the condition is known as *bullous emphysema*. These bullae may further enlarge and rupture into pleural space leading to pneumothorax.

**CASE 2: CONSOLIDATION OF THE LUNG (FIG. 1.2)**

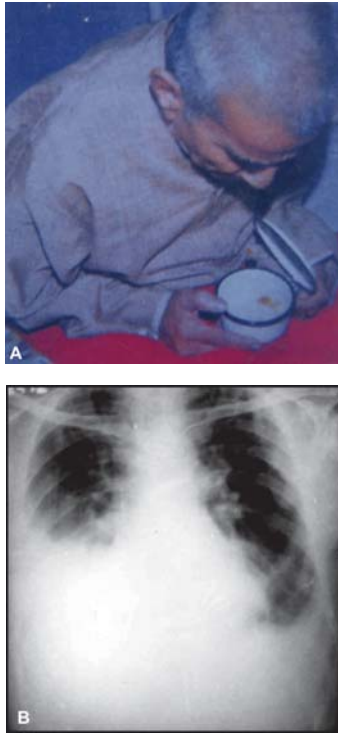
The patient (Fig. 1.2A) presented with fever, cough, haemoptysis with rusty sputum and pain chest increasing during respiration of 2 weeks duration.

**Points to be Noted in History and Their Relevance**

- Recent travel, local epidemics around point source suggest legionella as the cause in middle to old age.
- Large scale epidemics, associated sinusitis, pharyngitis, laryngitis suggest chlamydia infection.
- A patient with underlying lung disease (bronchiectasis, fibrosis) with purulent sputum suggest secondary pneumonia (bronchopneumonia).
- History of past epilepsy, recent surgery on throat suggest aspiration pneumonia.
- Co-existent debilitating illness, osteomyelitis or abscesses in other organs may lead to staphylococcal consolidation.
- Contact with sick birds, farm animals suggest *chlamydia psittaci* and *coxiella burnetii* pneumonia.
- History of smoking suggest malignancy
- Recurrent episodes suggest secondary pneumonia
- History of diabetes, intake of steroids or antimetabolic drugs, AIDS suggest pneumonia in immunocompromised host.

**Physical Signs***General Physical*

- Toxic look
- Fever present
- Tachypnoea present
- Tachycardia present
- Cyanosis absent
- Herpes labialis may be present
- Neck stiffness absent, if present suggests meningitis as a complication



**Figs 1.2A and B: Pneumonic consolidation: A. A patient with pneumonia having haemoptysis; B. Chest X-ray showing right lower lobe consolidation**

**Clinical Presentations**

- Short history of fever with chills and rigors, cough, often pleuritic chest pain which is occasionally referred to shoulder or anterior abdominal wall is a classic presentation of a patient with pneumonic consolidation in young age. In children, there may be associated vomiting and febrile convulsions.
- A patient may present with symptoms of complications, i.e. pleural effusion (dyspnoea, intractable cough, heaviness of chest), meningitis (fever, neck pain, early confusion or disorientation, headache, violent behaviour, convulsions, etc.)
- A patient with malignant consolidation presents with symptoms of cough, pain chest, dyspnoea, haemoptysis, weight loss, etc. Associated symptoms may include hoarseness of voice, dysphagia, fever, weight loss, and loss of appetite. These patients are old and usually smokers.

**Systemic Examination***Inspection*

- Shape of chest is normal
- Movements of the chest reduced on the side involved due to pain
- In this case (Fig. 1.2), movements of right side of the chest will be reduced.
- Trachea central
- Apex beat normal
- No indrawing of intercostal spaces; and accessory muscles of respiration are not working (active).

*Palpation*

- Restricted movement on the side involved (right side in this case)
- Reduced expansion of the chest (right side in this case)
- Trachea and apex beat normal in position
- Tactile vocal fremitus is *increased* on the side and over the part involved (in this case, apparent in right axilla and front of central part of right chest).
- *Friction rub* may be palpable over the part of the chest involved.

*Percussion*

- Dull percussion note on the side and over the part of the chest involved (right axilla and right lower anterior chest in this case).

*Auscultation*

The following findings will be present on the side and part involved (right axilla and right lower anterior chest in this case).

- Bronchial breath sounds
- Increased vocal resonance with *bronchophony* and *whispering pectoriloquy*.
- Aegophony
- Pleural rub

*Note:* As the lung is solidified, no crackles or wheeze will be heard at present, but during resolution, crackles will appear due to liquefaction of the contents.



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### 16. What is the provisional diagnosis? And why?

**Ans.** The provisional clinical diagnosis in this case is right pneumonic consolidation because of short duration of classic triad of symptoms (fever, cough, pleuritic chest pain) with all signs of consolidation on right side (read Table 1.1 for signs of consolidation).

### 17. What is the site of involvement?

**Ans.** Because all the signs are present in the right axilla and right lower anterior chest, hence, it is likely due to involvement of right middle and lower lobe.

### 18. What do you understand by the term consolidation? What are stages of pneumonia and their clinical characteristics?

**Ans.** Consolidation means solidification of the lung due to filling of the alveoli with inflammatory exudate. It represents second stage (red hepatisation) and third stage (grey hepatisation) of pneumonia (Table 1.6).

**Table 1.6:** Stages of pneumonia

Stage	Signs
I. Stage of congestion	Diminished vesicular breath sounds with fine inspiratory crackles due to alveolitis
II. Stage of red hepatisation	All signs of consolidation present as mentioned (Table 1.1).
III. Stage of grey hepatisation	— do—
IV. Stage of resolution	<ul style="list-style-type: none"><li>• Bronchial breathing during consolidation is replaced either by bronchovesicular or vesicular breathing.</li><li>• Mid-inspiratory and expiratory crackles (coarse crepitations) appear</li><li>• All other signs of consolidation disappear.</li></ul>

### 19. Patient has consolidation on X-ray but is asymptomatic. How do you explain?

**Ans.** Respiratory symptoms and signs in consolidation are often absent in elderly, alcoholics, immunocompromised and neutropenic patients.

*Note:* Children and young adults suffering from mycoplasma pneumonia may have consolidation with few symptoms and signs in the chest, i.e. there is discrepancy between symptoms and signs with radiological

appearance of consolidation. Deep seated consolidation or consolidation with non-patent bronchus may not produce physical signs on chest examination.

### 20. What are the common sites of aspiration pneumonia?

**Ans.** The site of aspiration depends on the position of patient (Table 1.7)

**Table 1.7:** Aspiration during supine and upright position

Aspiration during supine position	Aspiration in upright position
<ul style="list-style-type: none"><li>• Posterior segment of the upper lobe and superior segment of the lower lobe on the right side (right is more involved than left side)</li></ul>	<ul style="list-style-type: none"><li>• Basilar segments of both lower lobes</li></ul>

### 21. What are the causes of consolidation?

**Ans.** Main causes of consolidation are as follows:

1. Pneumonic (lobar consolidation), may be bacterial, viral, fungal, allergic, chemical and radiation induced. Tuberculosis causes apical consolidation.
2. Malignant (bronchogenic carcinoma)
3. Following massive pulmonary infarct (pulmonary embolism – may cause collapse consolidation).

### 22. How pneumonia in young differs from pneumonia in old persons?

**Ans.** Pneumonia in young and old persons are compared in Table 1.8.

### 23. How do you classify pneumonias?

**Ans.** Pneumonias can be classified in various ways;

#### I. Depending on the immunity and host resistance

- Primary (normal healthy individuals)
- Secondary (host defence is lowered). It further includes;
  - Acute bronchopneumonia (lobar, lobular, or hypostatic)
  - Aspiration pneumonia
  - Hospital-acquired pneumonia (nosocomial)
  - Pneumonias in immunocompromised host
  - Suppurative pneumonia including lung abscess.

#### II. Anatomical classification

- Lobar

**Table 1.8:** Differentiating features of pneumonia in younger and older persons

<i>Pneumonia in young</i>	<i>Pneumonia in old</i>
<ul style="list-style-type: none"> <li>Primary (occurs in previously healthy individuals)</li> <li>Common organisms are; <i>pneumococci</i>, <i>mycoplasma</i>, <i>chlamydia</i>, <i>coxiella</i></li> <li>Florid symptoms and signs</li> <li>Systemic manifestations are less pronounced</li> <li>Complications are less frequent</li> <li>Resolution is early</li> <li>Response to treatment is good and dramatic</li> </ul>	<ul style="list-style-type: none"> <li>Secondary (previous lung disease or immunocompromised state)</li> <li>Common organisms are; <i>pneumococci</i>, <i>H. influenzae</i>, <i>legionella</i></li> <li>Few or no symptoms and signs</li> <li>More pronounced systemic features</li> <li>Complications are frequent</li> <li>Resolution may be delayed</li> <li>Response to treatment is slow</li> </ul>

- Lobular (bronchopneumonia, bilateral)
- Segmental (hypostatic pneumonia).

**III. Aetiological classification**

- Infective, e.g. bacterial, viral, mycoplasma, fungi, protozoal, pneumocystis carinii
- Chemical – induced (lipoid pneumonia, fumes, gases, aspiration of vomitus)
- Radiation
- Hypersensitivity/ allergic reactions.

**IV. Empiricist's classification (commonly used)**

- *Community-acquired pneumonia* (*S. pneumoniae*, *Mycoplasma*, *Chlamydia*, *legionella*, *H. influenzae*, virus, fungi, anaerobes, mycobacterium)
- *Hospital-acquired pneumonia* (*Pseudomonas*, *B. proteus*, *Klebsiella*, *Staphylococcus*, oral anaerobes)
- *Pneumonia in immunocompromised host* (*Pneumocystis carinii*, *Mycobacterium*, *S. pneumoniae*, *H. influenzae*).

**24. What are the characteristics of viral pneumonia?**

**Ans.** Characteristics of viral pneumonia are as follows:

- Constitutional symptoms, e.g. headache, malaise, myalgia, anorexia are predominant (commonly due to *influenza*, *parainfluenza*, *measles* and *respiratory syncytial virus*).

- There may be no respiratory symptoms or signs and consolidation may just be discovered on chest X-ray
- Cough, at times, with mucoid expectoration.
- Haemoptysis, chest pain (pleuritic) and pleural effusion are rare
- Paucity of physical signs in the chest
- Chest X-ray shows reticulonodular pattern instead of lobar consolidation
- Spontaneous resolution with no response to antibiotics
- WBC count is normal.

**25. What are the characteristics of various bacterial pneumonias?**

**Ans.** Characteristics of bacterial pneumonias are enlisted in Table 1.9.

**26. What are the complications of pneumonia?**

**Ans.** Common complications of pneumonia are;

- Pleural effusion and empyema thoracis
- Lung abscess
- Pneumothorax
- Meningitis
- Circulatory failure (Waterhouse – Friedrichson's syndrome)
- Septic arthritis
- Pericarditis
- Peritonitis
- Peripheral thrombophlebitis
- Herpes labialis (secondary infection).

**27. What are the causes of recurrent pneumonia?**

**Ans.** Recurrent pneumonias mean two or more attacks within a few weeks. It is due to either reduced/lowered resistance or there is a local predisposing factor, i.e.

- Chronic bronchitis
- Hypogammaglobinaemia
- Pharyngeal pouch
- Bronchial tumour

**28. What is normal resolution? What is delayed resolution and nonresolution? What are the causes of delayed or non-resolution of pneumonia?**

**Ans.** Normal resolution in a patient with pneumonia means disappearance of symptoms and signs within two weeks of onset and radiological clearance within

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**Table 1.9:** Clinical and radiological features of bacterial pneumonias

<i>Pathogens</i>	<i>Clinical features</i>	<i>Radiological features</i>
<b>Common organisms</b>		
<i>Pneumococcal pneumonia</i>	Young to middle aged, rapid onset, high fever, chills, and rigors, pleuritic chest pain, herpes simplex labialis, <i>rusty</i> sputum. Toxic look, tachypnoea and tachycardia. All signs of consolidation present	Lobar consolidation (dense uniform opacity), one or more lobes
<i>Mycoplasma pneumoniae</i>	<ul style="list-style-type: none"> <li>Children and young adults (5-15 years), insidious onset, headache, systemic features. Often few signs in the chest. IgM cold agglutinins detected by ELISA</li> <li>Erythema nodosum, myocarditis, pericarditis rash, meningoencephalitis, hemolytic anaemia</li> </ul>	Patchy or lobar consolidation. Hilar lymphadenopathy present
<i>Legionella</i>	<ul style="list-style-type: none"> <li>Middle to old age, history of recent travel, local epidemics around point source, e.g. cooling tower, air conditioner</li> <li>Headache, malaise, myalgia, high fever, dry cough, GI symptoms</li> <li>Confusion, hepatitis, hyponatraemia, hypoalbuminaemia</li> </ul>	Shadowing continues to spread despite antibiotics and often slow to resolve
<b>Uncommon organisms</b>		
<i>H. influenzae</i>	<ul style="list-style-type: none"> <li>Old age, often underlying lung disease (COPD), purulent sputum, pleural effusion common</li> </ul>	Bronchopneumonia Signs of underlying disease present and are more pronounced
Staphylococcal pneumonia	<ul style="list-style-type: none"> <li>Occurs at extremes of ages, coexisting debilitating illness, often complicates viral infection</li> <li>Can arise from, or cause abscesses in other organs, e.g. osteomyelitis</li> <li>Presents as bilateral pneumonia, cavitation is frequent</li> </ul>	Lobar or segmental thin walled abscess formation (pneumatocoeles)
Klebsiella	Systemic disturbances marked, widespread consolidation often in upper lobes. Red-currant jelly sputum, lung abscess and cavitation frequent	Consolidation with expansion of the affected lobes, bulging of interlobar fissure

four weeks. Delayed resolution means when physical signs persist for more than two weeks and radiological findings persist beyond four weeks after proper antibiotic therapy. Causes are;

- Inappropriate antibiotic therapy
- Presence of a complication (pleural effusion, empyema)
- Depressed immunity, e.g. diabetes, alcoholism, steroids therapy, neutropenia, AIDS, hypogammaglobulinaemia
- Partial obstruction of a bronchus by a foreign body like denture or malignant tumour
- Fungal or atypical pneumonia
- Pneumonia due to SLE and pulmonary infarction or due to recurrent aspirations in GERD or Cardia achalasia.

*Non-resolution* means radiological findings persisting beyond eight weeks after proper antibiotic therapy.

Causes are;

- Neoplasm
- Underlying lung disease, e.g. bronchiectasis

- Virulent organisms, e.g. Staphylococcus, Klebsiella
- Underlying diabetes
- Old age.

### 29. How do you diagnose pleural effusion in a patient with consolidation?

**Ans.** The clues to the diagnosis are:

- History suggestive of pneumonia (fever, pain chest, haemoptysis, cough) and persistence of these symptoms beyond 2-4 weeks
- Signs of pleural effusion, e.g. stony dull percussion note, shifting of trachea and mediastinum.
- The obliteration of costophrenic angle in presence of consolidation on chest X-ray.

### 30. What is the mechanism of trachea being shifted to same side in consolidation?

**Ans.** Usually, trachea remains central in a case of consolidation but may be shifted to the same side if;

- Consolidation is associated with collapse on the same side (Collapse consolidation due to malignancy)
- Consolidation is associated with underlying old fibrosis on the same side.

### 31. What is typical or atypical pneumonia syndrome?

**Ans.** The *typical pneumonia syndrome* is characterised by sudden onset of fever, productive cough, pleuritic chest pain, signs of consolidation in the area of radiological abnormality. This is caused by *S. pneumoniae*, *H. influenzae*, *oral anaerobes* and *aerobes* (mixed flora).

The *atypical pneumonia syndrome* is characterised by insidious onset, a dry cough, predominant extra-pulmonary symptoms such as headache, myalgia, malaise, fatigue, sore throat, nausea, vomiting and diarrhoea, and abnormalities on the chest X-ray despite minimal or no physical signs of pulmonary involvement. It is produced by *M. pneumoniae*, *L. pneumophila*, *P. carinii*, *S. pneumoniae*, *C. psittaci*, *Coxiella burnetii* and some fungi (*H. capsulatum*).

### 32. What will be the features in malignant consolidation?

**Ans.** Common features in malignant consolidation are;

- Patient will be old and usually smoker

- History of dry persistent hacking cough, dyspnoea, haemoptysis, pleuritic chest pain.
- There will be weight loss, emaciation due to malignant cachexia.
- Cervical lymphadenopathy may be present.
- Trachea will be central, i.e. but is shifted to same side if there is associated collapse or to the opposite if associated with pleural effusion.
- All signs of consolidation, i.e. diminished movements, reduced expansion, dull percussion note, bronchial breathing may be present if bronchus is occluded. The bronchial breathing is from the adjoining patent bronchi. The bronchial breathing will, however, be absent if there is partial bronchial obstruction.
- Signs and symptoms of local spread, i.e. pleura (pleural effusion), to hilar lymph nodes (dysphagia due to oesophageal compression, dysphonia due to recurrent laryngeal nerve involvement, diaphragmatic paralysis due to phrenic nerve involvement, superior vena cava compression), brachial plexus involvement (i.e. pancoast tumour producing monoplegia), cervical lymphadenopathy (Horner's syndrome—cervical sympathetic compression) may be evident.
- Sometimes, signs of distant metastases, e.g. hepatomegaly, spinal deformities, fracture of rib(s) are present.

### 33. What are the pulmonary manifestations of bronchogenic carcinoma?

**Ans.** It may present as;

- Localised *collapse* of the lung due to partial bronchial obstruction.
- *Consolidation* – a solid mass lesion
- *Cavitation* Secondary degeneration and necrosis in a malignant tumour leads to a cavity formation.
- *Mediastinal syndrome* It will present with features of compression of structures present in various compartments of mediastinum (superior, anterior, middle and posterior). These include;
  - *Superior vena cava obstruction* with oedema of face, suffused eyes with chemosis, distended nonpulsatile neck veins, and prominent veins over the upper part of the chest as well as forehead.

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(Read case discussion on superior mediastinal compression).

- Dysphonia and bovine cough due to compression of recurrent laryngeal nerve, stridor due to tracheal obstruction
- Dysphagia due to oesophageal compression
- Diaphragmatic paralysis – phrenic nerve compression
- Intercostal neuralgia due to infiltration of intercostal nerves
- Pericardial effusion due to infiltration of pericardium, myocarditis (arrhythmias, heart failure).
- Thoracic duct compression leading to chylous pleural effusion
- Brachial plexus compression (pancoast tumour) producing monoplegia

### 34. What are the extrapulmonary nonmetastatic manifestations of carcinoma lung?

**Ans.** The paraneoplastic/nonmetastatic extrapulmonary manifestations occur in patients with oat cell carcinoma and are not due to local or distant metastatic spread. These are;

- A. Endocrinal (hormones produced by the tumour)
- ACTH—Cushing's syndrome
  - PTH—Hypercalcaemia
  - ADH—Hyponatraemia
  - Insulin-like peptide—Hypoglycaemia
  - Serotonin—Carcinoid syndrome

Erythropoietin—Polycythaemia

Sex hormone—Gynaecomastia

- B. Skeletal – Digital clubbing
- C. Skin, e.g. Acanthosis nigricans, pruritus
- D. Neurological
- Encephalopathy
  - Myelopathy
  - Myopathy
  - Amyotrophy
  - Neuropathy
- E. Muscular
- Polymyositis, dermatomyositis
  - Myasthenia –myopathic syndrome (*Lambert-Eaton syndrome*)
- F. Vascular
- Migratory thrombophlebitis
- G. Hematological
- Hemolytic anaemia
  - Thrombocytopenia

### 35. Where do the distant metastases occur in bronchogenic carcinoma

**Ans.** It spreads to distant organs in three ways;

- Lymphatic spread involves mediastinal, cervical and axillary lymph nodes
- Hematogenous spread involves liver, brain, skin, bone and subcutaneous tissue
- Transbronchial spread leads to involvement of other side.



### CASE 3: PLEURAL EFFUSION AND EMPYEMA THORACIS

The patient (Fig. 1.3B) presented with fever, pain chest, dyspnoea for the last 1 month. No associated cough or haemoptysis.

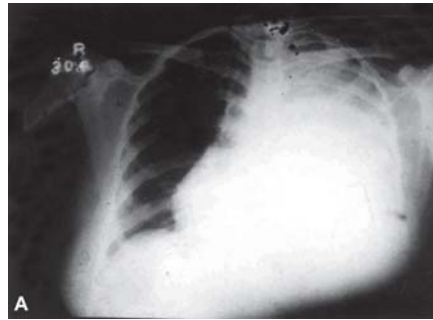
#### Points to be Noted in History

- History of fever, cough, rigors, removal of fluid in the past
- History of trauma
- Past/present history of tuberculosis, malignancy
- Occupational history
- Any skin rash, swelling of joints, lymphadenopathy
- Any history of dysentery in the past
- Haemoptysis
- Is there history of oedema, pain abdomen, distension of abdomen (ascites), oedema legs
- Any menstrual irregularity in female

#### Treatment History

#### General Physical Examination (GPE)

- Any puffiness of face or malar flush or rash
- Fever
- Tachypnoea
- Tachycardia
- Patient prefers to lie in lateral position on uninvolved side
- Emaciation
- Cervical lymph nodes may be palpable if effusion is tubercular
- Neck veins may be full due to kinking of superior vena cava
- Signs of underlying cause
- Oedema may be present if pleural effusion is due to systemic disorder
- Look for any rash, arthritis/arthralgia
- Note the vitals, pulse, BP, temperature and respiration.



**Figs 1.3A and B:** Pleural effusion left side: A. Chest X-ray; B. Fluid drainage

#### Presenting symptoms

- Fever, non-productive cough and pleuritic chest pain
- Heaviness/tightness of chest in massive effusion
- Dyspnoea due to compression collapse of the lung by large amount of fluid and shift of the mediastinum to opposite side leading to reduction of vital capacity

#### Systemic Examination

##### Inspection

- Increased respiratory rate
- Restricted respiratory movement on affected side (left side in this case)
- Intercostal spaces are full and appear widened on the affected side (left side in this case)

##### Palpation

- Diminished movement on the side involved (left side in this case)
- Chest expansion on measurement is reduced
- Trachea and apex beat (mediastinum shifted to opposite side (right side in this case)
- Vocal fremitus reduced or absent on affected side (left side in this case)
- No tenderness
- Occasionally, in early effusion, pleural rub may be palpable

##### Percussion

- Stony dull note over the area of effusion on the affected side (left side in this case)
- Rising dullness in axilla (S-shaped Ellis' curve) due to capillary action
- Skodiac band of resonance at the upper level of effusion because of compensatory emphysema
- Traube's area is dull on percussion
- No shifting dullness
- No tenderness

##### Auscultation

- Breath sounds are absent over the fluid (left side in this case)
- Vocal resonance is reduced over the area of effusion (left side in this case)
- Sometimes, bronchial breathing (tubular – high pitched, bronchophony and whispering pectoriloquy and aegophony present at the upper border (apex) of pleural effusion (left inter-scapular region in this case)
- Pleural rub can be heard in some cases



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### 36. What do you understand by pleural effusion?

**Ans.** Normal pleural space on each side contains 50-150 ml of fluid but excessive collection of fluid above the normal value is called *pleural effusion* which may or may not be detected clinically. Fluid between 150-300 ml can be detected radiologically by chest X-ray (obliteration of costophrenic angle). More than 500 ml fluid can be detected clinically.

*Note* USG of the chest is the earliest means of detecting the small amount of fluid.

### 37. What are the causes of pleural effusion?

**Ans.** Pleural fluid may be clear (hydrothorax) or turbid (pyothorax), may be blood stained (haemorrhagic) or milky white (chylous).

Biochemically, the fluid may be transudate or exudate; the differences between the two are summarised in Table 1.10. The diagnosis of various types of fluid are given in Table 1.11.

Various types of effusions and their causes are given in Table 1.12.

**Table 1.10:** Characteristics of pleural fluid

Fluid	Transudate (SFAG > 1.1)	Exudate (SFAG < 1.1)
1. Appearance	Clear, light yellow	Straw-coloured, turbid or purulent, milky or haemorrhagic
2. Protein	< 3 g% or <50% of serum proteins	>3 g% or >50% of serum proteins
3. Serum/fluid albumin gradient	>1.1	<1.1
4. Glucose	Normal	Low
5. pH	>7.3	<7.3
6. Cells (WBCs)	<1000/mm <sup>3</sup>	Usually >1000/mm <sup>3</sup>
7. Fluid LDH	<2/3rd of serum LDH	>2/3rd of serum LDH
8. Fluid/serum LDH ratio	<0.6	>0.6
9. Fluid deaminase levels	Low	High
10. Fluid cholesterol	Low	High
11. Culture	Sterile	May yield organisms

SFAG = Serum / fluid albumin gradient.

**Table 1.11:** Causes of pleural effusion depending on the fluid characteristic

Common	Uncommon
<b>I. Transudate (SFAG &gt; 1.1)</b>	
<ul style="list-style-type: none"> <li>Congestive heart failure</li> <li>Cirrhosis of liver</li> <li>Nephrotic syndrome</li> <li>Hypoproteinaemia due to any cause</li> <li>Pericardial effusion</li> </ul>	<ul style="list-style-type: none"> <li>Superior vena cava obstruction</li> <li>Myxoedema</li> <li>Pulmonary emboli</li> <li>Peritoneal dialysis</li> </ul>
<b>II. Exudate (SFAG &lt; 1.1)</b>	
<ul style="list-style-type: none"> <li>Infections e.g. tubercular, bacterial (pneumonia), viral</li> <li>Malignancy, e.g. bronchogenic (common), mesothelioma (rare)</li> <li>Collagen vascular disorders e.g. SLE, rheumatoid arthritis, Wegener's granulomatosis</li> <li>Pericarditis</li> <li>Meig's syndrome</li> <li>Sarcoidosis</li> <li>Asbestosis</li> <li>Ruptured liver abscess into pleural space</li> </ul>	<ul style="list-style-type: none"> <li>Chylothorax</li> <li>Pancreatitis</li> <li>Esophageal perforation</li> <li>Subphrenic abscess</li> <li>Post-cardiac injury syndrome</li> <li>Uraemia</li> <li>Radiation injury</li> <li>Iatrogenic</li> <li>Drug-induced effusion, e.g. Nitrofurantoin</li> <li>Dantrolene</li> <li>Methysergide</li> <li>Bromocriptine</li> <li>Procarbazine</li> <li>Amiodarone</li> </ul>

### 38. What are causes of unilateral, bilateral and recurrent pleural effusion?

**Ans.** Causes of various types of pleural effusion are given in Table 1.12:

#### I. Bilateral pleural effusion. The causes are;

- Congestive heart failure
- Collagen vascular diseases, e.g. SLE, rheumatoid arthritis
- Lymphoma and leukaemias
- Bilateral tubercular effusion (rare)
- Pulmonary infarction

#### II. Unilateral pleural effusion. The causes are;

##### Right-sided effusion

- Rupture of acute amoebic liver abscess into pleura
- Cirrhosis of the liver
- Congestive cardiac failure
- Meig's syndrome—fibroma of ovary with pleural effusion and ascites

**Table 1.12:** Various types of fluids and their causes

*Chylous (milky) effusion* (Triglyceride > 1000 mg% with many large fat globules)

- Nephrotic syndrome
- Tubercular
- Malignancy
- Lymphoma
- Filariasis
- Myxoedema
- Trauma to chest wall

**Ether extraction dissolves fat and leads to clearing; confirms true chylous nature of fluid.**

*Chyliform* (fat present is not derived from thoracic duct but from degenerated leucocytes and tumour cells). The fat globules are small. Causes are:

- Tubercular
- Carcinoma of lung and pleura

*Pseudochylous*. Milky appearance is not due to fat but due to albumin, calcium, phosphate and lecithine. Causes are;

- Tuberculosis
- Nephrosis
- Heart disease
- Malignancy

**Alkalinisation dissolves cellular protein and clears the fluid thus differentiates it from true chylous**

*Cholesterol effusion* (Glistening opalescent appearances of fluid due to cholesterol crystals). Causes are;

- Long standing effusion, e.g. tuberculosis, carcinoma, nephrotic syndrome, myxoedema and post-myocardial infarction.

*Haemorrhagic effusion* (Hemothorax, e.g. blood stained fluid or fluid containing RBCs)

- Neoplasm, e.g. primary or secondary pleural mesothelioma
- Chest trauma (during paracentesis)
- Tubercular effusion
- Leukaemias and lymphoma
- Pulmonary infarction
- Bleeding diathesis
  - Anticoagulant therapy
  - Acute haemorrhagic pancreatitis

### III. Causes of recurrent pleural effusion

- Malignancy lung (e.g. bronchogenic, mesothelioma)
- Pulmonary tuberculosis
- Congestive heart failure
- Collagen vascular disorder

### 39. What is empyema thoracis? What are its causes?

**Ans.** Collection of pus or purulent material in the pleural cavity is called *empyema thoracis*.

The causes are:

1. *Diseases of the lung* (Infection travels from the lung to the pleura either by contiguity or by rupture)
  - Lung abscess
  - Pneumonia
  - Tuberculosis
  - Infection
  - Bronchiectasis
  - Bronchopleural fistula
2. *Diseases of the abdominal viscera* (spread of infection from abdominal viscera to pleura)
  - Liver abscess (ruptured or unruptured)
  - Subphrenic abscess
  - Perforated peptic ulcer
3. *Diseases of the mediastinum* There may be infective focus in the mediastinum from which it spreads to the pleura.
  - Cold abscess
  - Oesophageal perforation
  - Osteomyelitis
4. Trauma with superadded infection
  - Chest wall injuries (gun-shot wound, stab wound)
  - Postoperative
5. *Iatrogenic* Infection introduced during procedure.
  - Chest aspiration
  - Liver biopsy
6. *Blood-borne infection* e.g. septicemia.

### 40. What are physical signs of empyema thoracis?

**Ans.**

- Patient has a toxic look and prostration
- Signs of toxemia (fever, tachypnoea and tachycardia). There is hectic rise of temperature with chills and rigors.
- Digital clubbing may be evident
- Intercostal spaces are full and may be tender
- All signs of pleural effusion will be present except rising dullness in axilla. This is due to collection of thick pus rather than clear fluid which does not obey the law of capillary action.
- The skin is red, oedematous and glossy overlying empyema of recent onset. There may be a scar mark of an intercostal drainage (tube aspiration).
- Rarely, a subcutaneous swelling on the chest wall may be seen called *empyema necessitans*. The swelling increases with coughing.

**Tip:** The presence of signs of toxæmia (toxic look, fever, tachypnoea, tachycardia, sweating) in a patient with pleural effusion indicates *empyema thoracis*

### 41. What is massive pleural effusion?

**Ans.** It refers to a large collection of fluid causing gross shifting of the mediastinum to the opposite side with stony dull note extending upto 2nd intercostal space or above on front of the chest.

### 42. What is phantom tumour?

**Ans.** This is nothing but an interlobar effusion (effusion in interlobar fissure) producing a rounded homogenous opacity on chest X-ray. This mimics a tumour due to its dense opacity but disappears with resolution of effusion, hence, called *phantom tumour*. This is occasionally seen in patients with congestive heart failure and disappears with diuretic therapy.

### 43. What is subpulmonic effusion? How will diagnose it?

**Ans.** A collection of fluid below the lung and above the diaphragm is called *subpulmonic effusion*. This is suspected when diaphragm is unduly elevated on that side on chest X-ray. Chest X-ray taken in lateral decubitus position shows pleural effusion (layering out of the opacity along the lateral chest wall) which confirms the diagnosis.

### 44. How do you explain the position of trachea either as central or to the same side in a case with pleural effusion?

**Ans.** Remember that negative intrapleural pressure on both sides keeps the trachea central, but, it is shifted to opposite side when a positive pressure develops in one of the interpleural space, therefore, midline trachea despite pleural effusion on one side could be due to?

- Mild pleural effusion (insignificant positive pressure develops)
- Loculated or encysted pleural effusion (positive pressure develops but not transmitted to opposite side—no pushing effect).
- Bilateral pleural effusion (both pleural cavities have positive pressure that neutralise each other's effect)
- Pleural effusion associated with apical fibrosis (fibrosis pulls the trachea to same side and neutralises the pushing effect of pleural effusion on the same side)

- Malignant pleural effusion with absorption collapse due to endobronchial obstruction. Due to collapse, trachea tries to shift towards the same side but pushing effect of effusion keeps it central in position.
- Collapse consolidation due to any cause (Isolated collapse and isolated consolidation has opposing effects).

Trachea can be shifted to same side in a case of effusion, if an underlying lung disease (e.g. collapse or fibrosis on the same side) exerts a pulling effect on the trachea and overcomes the pushing effect of effusion.

### 45. What are signs at the apex (upper level) of pleural effusion?

**Ans.** The following signs develops only and occasionally in moderate (500-1000 ml) pleural effusion.

- Rising dullness; S-shaped Ellis curve in axilla
- Skodiac resonance – a band of hyper-resonance due to compensatory emphysema
- Bronchial breathing – high pitched tubular with bronchophony, whispering pectoriloquy and aegophony
- Pleural rub – rarely

### 46. What are the causes of recurrent filling of pleural effusion after paracentesis?

**Ans.** Recurrent filling of the pleural effusion means appearance of the fluid to same level or above it on X-ray chest within few days (rapid filling) to weeks (slow filling) after removal of the fluid. That is the reason, a chest X-ray is taken before and after removal of the fluid to know the result of the procedure, its complications and later on its refilling. The causes are;

1. Rapid refilling of pleural effusion
  - Malignancy
  - Acute tuberculosis
2. Slow refilling
  - Tubercular effusion on treatment
  - Congestive cardiac failure – slow response or no response to conventional diuretics
  - Collagen vascular disorders
  - Meig's syndrome

### 47. What are the complications of pleural effusion?

**Ans.** Common complications of pleural effusion are;

- **Thickened pleura** (indicates healed pleural effusion)

- **Empyema thoracis** – spontaneous or iatrogenic (during tapping of effusion with introduction of infection with improperly sterilised needle)
- **Nonexpansion of the lung.** Usually, after removal of pleural fluid, there is re-expansion of the compressed lung immediately, but sometimes in long standing cases, it may not occur due to underlying fibrosis.
- **Acute pulmonary oedema** is a procedural complication, develops with sudden withdrawal of a large amount of fluid. It is uncommon.
- **Hydropneumothorax** is again iatrogenic (procedural complication) due to lung injury and leakage of air into pleural space during pleural aspiration. To know this complication, a repeat X-ray chest is necessary after aspiration.
- **Cachexia** may develop in long-standing and malignant pleural effusion.

#### 48. What are causes of lymphadenopathy with pleural effusion?

**Ans.** Common causes are:

- Tubercular lymphadenitis with pleural effusion (lymph node in cervical, axillary, mediastinal regions may be enlarged)
- Lymphomas (effusion with generalised lymphadenopathy and splenomegaly)
- Acute lymphoblastic leukaemia (cervical and axillary lymph nodes enlargement)
- Malignancy lung (scalene node, Virchow's gland, mediastinal lymph node)
- Collagen vascular disorder (generalised lymphadenopathy)
- Sarcoidosis (cervical, bilateral hilar lymphadenopathy).

#### 49. What are differences between tubercular and malignant pleural effusion?

**Ans.** Tubercular and malignant pleural effusions are differentiated in Table 1.13.

#### 50. How will you investigate a case of pleural effusion?

**Ans.** A pleural effusion being of varied aetiology, needs investigations for confirmation of the diagnosis as well as to find out the cause.

**Table 1.13:** Differentiating features of tubercular and malignant pleural effusion

Tubercular	Malignant
<b>A. Clinical characteristics</b>	
<ul style="list-style-type: none"> <li>• Commonest cause of effusion in all age groups</li> <li>• Slow, insidious onset, can be acute or sudden</li> <li>• Slow filling</li> <li>• Cough, fever (evening rise), hemoptysis, night sweats are common complaints</li> <li>• Cervical, axillary lymph nodes may be enlarged</li> <li>• Weakness, loss of weight present</li> <li>• Clubbing uncommon</li> <li>• No signs of local compression</li> </ul>	<ul style="list-style-type: none"> <li>• Common cause in old age</li> <li>• Acute sudden onset</li> <li>• Rapid filling</li> <li>• Cough, hemoptysis, dyspnoea, tightness of chest, hoarseness of voice are presenting symptoms</li> <li>• Scalene nodes or Virchow's gland enlarged</li> <li>• Marked cachexia and prostration</li> <li>• Clubbing common</li> <li>• Signs of local compression e.g. superior vena cava (prominent neck vein and chest veins), trachea (dysphonia, oesophagus dysphagia, and phrenic nerve diaphragmatic paralysis) may be accompanying symptoms</li> </ul>
<ul style="list-style-type: none"> <li>• Localised crackles or rhonchi may be present depending on the site and type of lung involvement</li> </ul>	<ul style="list-style-type: none"> <li>• Localised wheeze or rhonchi common than crackles</li> </ul>
<b>B. Fluid characteristics</b>	
<ul style="list-style-type: none"> <li>• Straw-coloured exudate</li> <li>• Lymphocytes present</li> </ul>	<ul style="list-style-type: none"> <li>• Hemorrhagic, exudate</li> <li>• Malignant cells may be present along with RBCs</li> </ul>
<ul style="list-style-type: none"> <li>• Cob-web coagulum on standing</li> </ul>	<ul style="list-style-type: none"> <li>• RBCs may settle down on standing if haemorrhagic</li> </ul>

1. **Routine blood tests** (TLC, DLC and ESR). High ESR and lymphocytosis go in favour of tubercular effusion.
2. **Blood biochemistry**
  - Serum amylase for pancreatitis
  - Autoantibodies for collagen vascular disorders
  - Rheumatoid factor for rheumatoid arthritis
3. **Chest X-ray** (PA view, Fig. 1.3A) shows;
  - A lower homogenous opacity with a curved upper border which is concave medially but rising laterally towards the axilla.
  - Obliteration of costophrenic angle. It is the earliest sign hence, present in all cases of pleural effusion

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irrespective of its cause except loculated or encysted effusion.

- Shift of trachea and mediastinum to opposite side
- Lateral view is done to differentiate it from lobar consolidation
- Lateral decubitus view is taken in case of subpulmonic effusion
- Repeat X-ray chest after therapeutic aspiration of fluid

4. *Sputum examination*

- For AFB and malignant cells

5. *Mantoux test*. It is not much of diagnostic value, may be positive in tuberculosis, negative in sarcoidosis, lymphoma and disseminated (miliary) tuberculosis or tubercular effusion in patients with AIDS.

6. *FNAC of lymph node*, if found enlarged

7. *Ultrasonography* is done to confirm the diagnosis and to mark the site for aspiration, and to find out the cause

8. *CT scan and MRI* are usually not required for diagnosis, but can be carried out to find out the cause wherever appropriate, and to differentiate localised effusion from pleural tumour.

9. *Aspiration of pleura fluid for;*

Confirmation of diagnosis. At least 50 ml of fluid is to be removed and subjected to

- biochemistry (transudate/exudate)
- cytology (for malignant cells, RBCs, WBCs)
- smear examination (e.g. Gram' stain, Ziehl-Neelsen stain, special stains for malignant cells)
- Culture for AFB. Recently introduced BACTEC system gives result within 7 days.
- For indications of pleural aspiration, read bedside procedures and instruments used.

10. *Bronchoscopy* in a suspected case of bronchogenic carcinoma

11. *Pleural biopsy* to find out the cause

12. *Thoracoscopy* to inspect the pleura so as to find out the cause. It is done rarely.



## CASE 4: PNEUMOTHORAX

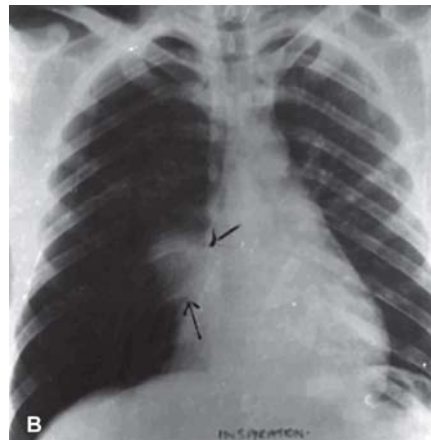
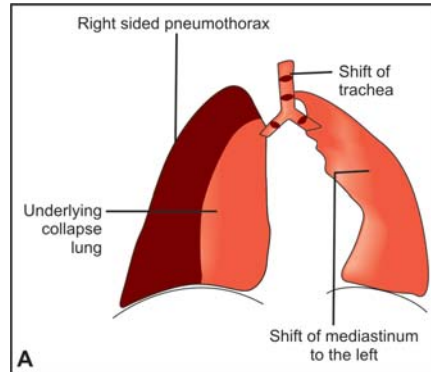
The patient whose X-ray is depicted in Figure 1.4B presented with acute severe dyspnoea, tachypnoea and tachycardia of few days duration. The patient was cyanosed and was admitted as an emergency.

### Points to be Stressed in History

- Past/present history of COPD, tuberculosis, haemoptysis or trauma
- History of similar episodes in the past
- Any history of IHD (chest pain in the present or past)
- Any history of prolonged immobilisation or calf pain (pulmonary thromboembolism)

### General Physical Examination

- Posture. Patients prefer to lie on the uninvolved side in lateral decubitus position or propped up position.
- Restlessness.
- Tachypnoea (respiratory rate is increased), dyspnoea at rest
- Tachycardia
- Central cyanosis, indicates tension pneumothorax
- Lymph nodes may or may not be palpable
- Trachea may be shifted to opposite side (sternomastoid sign or Trail's sign may be positive)
- Accessory muscles of respiration may be actively working
- Ear, nose, throat may be examined
- Note the vitals, i.e. pulse, BP, temperature and respiration. Presence of hypotension or shock indicates tension pneumothorax, creates an emergency situation and warrants removal of the air.



**Figs 1.4A and B: Pneumothorax: A. Diagrammatic illustration of pneumothorax; B. Chest X-ray showing right sided pneumothorax. The collapsed lung is indicated by arrows**

### Clinical Presentations

- Acute onset of dyspnoea at rest
- Associated pain chest or tightness of chest
- Symptoms non-progressive
- Palpitation and tachypnoea common
- Increasing breathlessness, cyanosis, tachycardia, tachypnoea, and hypotension suggest spontaneous tension pneumothorax
- Patient may have wheezing or other symptoms of COPD if it is the cause
- Cough aggravates breathlessness which is not relieved by any means except sitting posture

### Systemic Examination

#### Inspection

- Diminished movements on the side involved (right side in this case)
- Intercostal spaces widened and full on the side involved (right side in this case)
- Apex beat displaced to opposite side (left side in this case)
- Accessory muscles of respiration are hyperactive and stand out prominently in tension pneumothorax

#### Palpation

- Shift of trachea and apex beat (mediastinum) to the opposite side (e.g. left side in this case)
- Diminished movements on the side involved (e.g. right side)
- Expansion of chest decreased (on manual or tape measurement)
- Tactile vocal fremitus is reduced on the side involved (right side)

#### Percussion

- Hyper-resonant percussion note on the side involved (right side). It is a diagnostic sign and differentiates it from pleural effusion
- Obliteration of liver dullness if right side is involved (obliterated in this case), splenic dullness if left side is involved (not applicable in this case)

#### Auscultation

- Diminished vesicular breathing or absent breath sounds on the side involved (right side in this case). Bronchial breathing indicates bronchopleural fistula (open pneumothorax)
- Vocal resonance diminished over the area involved (right side)
- No adventitious sound

**Tip.** Silent hyper-resonant chest is characteristic of pneumothorax



**51. What is pneumothorax?**

**Ans.** Presence of air in the pleural cavity is called *pneumothorax*.

**52. How do you classify pneumothorax?**

**Ans.** The pneumothorax is divided into two categories; *spontaneous* and *traumatic*. The spontaneous pneumothorax may be primary (underlying lung is healthy) or secondary (occurs as a complication of some lung disease). The traumatic pneumothorax results from trauma (e.g. chest injury or procedural trauma). The causes of pneumothorax are given in Table 1.14.

**53. What are various types of pneumothorax and their clinical features?**

**Ans.** Table 1.15 discusses various types of pneumothorax and their clinical features.

**54. What are differences between a large air cyst or bulla and pneumothorax?**

**Ans.** Table 1.16 differentiates between bulla and pneumothorax.

**55. What is recurrent spontaneous pneumothorax?**

**Ans.** This refers to occurrence of second episode of pneumothorax within few weeks following the first episode. It occurs due to rupture of subpleural blebs or bullae in patients suffering from COPD. It is serious condition, needs chemical pleurodesis (instillation of kaolin, talcom, minocycline or 10% glucose into pleural space) or by surgical pleurodesis (achieved by pleural abrasions or parietal pleurectomy at thoracotomy or thoracoscopy). The causes of recurrent pneumothorax are given in Table 1.17.

**Caution** Patient who are at increased risk of developing recurrent pneumothorax after the first episode (e.g. flying or diving personnel) should undergo preventive treatment (respiratory exercises) after first episode. The respiratory exercises include to inflate air pillows, balloons or football bladder. It will also help to achieve expansion of the collapsed lung.

**56. What are the complications of pneumothorax?**

**Ans.** Common complications of pneumothorax are;

- Hydropneumothorax
- Empyema thoracis, pyopneumothorax
- Hemopneumothorax
- Thickened pleura

**Table 1.14:** Causes of pneumothorax**1. Spontaneous****A. Primary**

- Rupture of apical subpleural bleb or bulla in young patients
- Subpleural emphysematous bullae in old patients
- Rupture of the pulmonary end of pleuropulmonary adhesion. The risk factors for it include;
  - Tall body habitus
  - Smoking
  - Marfan's syndrome
  - Mitral valve prolapse
  - Going to high altitude
  - Bronchial anatomical abnormalities

**B. Secondary**

- COPD
- Pulmonary tuberculosis (subpleural focus) usually results in hydropneumothorax
- Infections, e.g. necrotising pneumonia, staphylococcal lung abscess, usually result in hydropneumothorax or pyopneumothorax
- Occupational lung disease, e.g. silicosis, coal-worker's pneumoconiosis
- Malignancy lung
- Interstitial lung disease
- Catamenial (endometriosis in females)
- Miscellaneous, e.g. oesophageal rupture, cystic fibrosis, Caisson's disease, asthma, pulmonary infarct, post radiation etc.

**2. Traumatic****Injury**

- Blunt injury to the chest or abdomen

**Iatrogenic (procedural)**

- Pleural tap
- Penetrating chest injury
- Pleural biopsy, lung biopsy
- Bronchoscopy, endoscopy and sclerotherapy

**3. Induced (artificial)**

- It was induced in the past to obliterate a tubercular cavity but is now obsolete term.

- Acute circulatory failure – cardiac tamponade in tension pneumothorax
- Atelectasis of the lung
- Surgical emphysema and pneumomediastinum.

**57. What do you understand by the term subcutaneous emphysema: What are its causes?**

**Ans.** Subcutaneous emphysema (or surgical emphysema – an older term) refers to presence of air in the subcutaneous space either formed by necrotising inflammation of the tissue by gas-forming organisms (gas gangrene) or by leakage of air from the lungs or neighbouring hollow structures. The causes are;

- Pneumothorax

**Table 1.15:** Types of pneumothorax and their clinical features

Feature	Closed (Fig. 1.4A)	Open	Tension (valvular)
Pathogenesis	The rupture site (opening gets closed and underlying lung is collapsed (deflated)). There is no communication between bronchus and the pleural space	The opening between the bronchus and pleural space does not close, remains patent, hence, called <i>bronchopleural fistula</i>	The communication between bronchus and pleural space persists and acts as a check valve (air can get in but cannot get out)
Mean pleural pressure	Negative (less than atmospheric pressure) hence, air can get absorbed and lung re-expands	Mean pleural pressure is atmospheric, hence, lung cannot re-expand. Secondly, due to patent communication, pneumothorax is likely to be infected leading to <i>pyopneumothorax</i> – a common complication	Mean pleural pressure is positive, hence, there is compression collapse of the underlying lung. It is an emergency situation because mean pleural pressure goes on building due to constant air entry during inspiration resulting in mediastinal shift and impaired venous return leading to cardiac tamponade requiring urgent drainage.
Causes	<ul style="list-style-type: none"> <li>• Rupture of subpleural bleb or emphysematous bullae</li> <li>• COPD</li> <li>• Spontaneous due to congenital bleb rupture</li> <li>• Rupture of pulmonary end of pleural adhesion</li> <li>• Secondary to lung disease</li> <li>• Chest injury</li> </ul>	<ul style="list-style-type: none"> <li>• Tubercular cavity</li> <li>• Lung abscess</li> <li>• Necrotising pneumonia</li> <li>• Chest trauma</li> <li>• Barotrauma</li> <li>• Empyema thoracic</li> <li>• Lung resection</li> </ul>	<ul style="list-style-type: none"> <li>• It can occur due to any cause</li> <li>• Catamenial pneumothorax (endometriosis in female)</li> </ul>
Symptoms	<ul style="list-style-type: none"> <li>• Mild cases may be asymptomatic and only chest X-ray may show pneumothorax</li> <li>• Some patients may present with breathlessness, pain chest/tightness of chest</li> <li>• Onset of dyspnoea may be acute or subacute</li> </ul>	<ul style="list-style-type: none"> <li>• Majority of patients with bronchopleural fistula present with cough, fever, mucopurulent or purulent expectoration. Dyspnoea is minimal.</li> <li>• Some complain of splash of fluid in the chest during jumping (e.g. hydropneumothorax)</li> </ul>	<ul style="list-style-type: none"> <li>• The presenting symptoms includes acute onset of dyspnoea, cough, tachypnoea, tachycardia</li> <li>• Cough worsens dyspnoea. No relieving factor known except sitting position</li> <li>• Hypotension or shock and central cyanosis may be present due to cardiac tamponade.</li> </ul>
Signs on the side involved	<ul style="list-style-type: none"> <li>• Reduced chest movement</li> <li>• Shift of trachea and mediastinum to opposite side</li> <li>• Hyper-resonant note</li> <li>• Markedly- diminished or absent breath sounds</li> <li>• Vocal fremitus and resonance are also reduced</li> <li>• <i>Coin test</i> is positive</li> </ul>	<ul style="list-style-type: none"> <li>• All signs of closed pneumothorax present <b>plus</b></li> <li>• Crack-pot sounds on percussion</li> <li>• Amphoric breath sounds with increased vocal resonance</li> <li>• Succussion splash indicates hydropneumothorax</li> <li>• Shifting dullness present if hydropneumothorax develops</li> <li>• <i>Coin test</i> may be positive</li> </ul>	<ul style="list-style-type: none"> <li>• All signs of closed pneumothorax present <b>plus</b></li> <li>• Dyspnoea, tachypnoea, tachycardia, cyanosis</li> <li>• Pulsus paradoxus</li> <li>• Neck veins full, markedly raised JVP</li> <li>• Hypotension</li> <li>• Obtunded consciousness</li> <li>• Progressive mediastinal shift to opposite side with labored respiration</li> </ul>
Plan of treatment	<ul style="list-style-type: none"> <li>• Observation till air is automatically absorbed</li> <li>• Water-seal drainage, if necessary</li> </ul>	<ul style="list-style-type: none"> <li>• Water seal drainage</li> <li>• Treat hydro or pyopneumothorax with proper antibiotic</li> <li>• Thoracic surgeon consultation should be sought</li> </ul>	<ul style="list-style-type: none"> <li>• Immediate relief can be given by putting a wide bore needle (No. 20) in second intercostal space in sitting position in mid-clavicular line on the side involved followed by water-seal drainage system.</li> <li>• Antitubercular drugs / antibiotic therapy as considered appropriate</li> <li>• O<sub>2</sub> inhalation and propped up position</li> <li>• Resuscitation of shock</li> <li>• Morphine 5-10 mg subcutaneous</li> </ul>

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**Table 1.16:** Differentiating features of bulla from pneumothorax

Large air cyst or bulla	Pneumothorax
May be congenital or acquired	Acquired usually
Mediastinum not shifted (trachea central)	Mediastinum shifted to opposite side (trachea shifted to opposite side)
No underlying collapse of the lung on chest X-ray	Collapse of the lung is demarcated from the pneumothorax by a thin line on chest X-ray

**Table 1.17:** Causes of recurrent pneumothorax

<ul style="list-style-type: none"> <li>• Rupture of apical subpleural bleb or emphysematous bullae.</li> <li>• Cystic fibrosis</li> <li>• Rupture of lung cysts</li> <li>• Rupture of bronchogenic carcinoma or oesophageal carcinoma</li> <li>• Catamenial pneumothorax</li> <li>• AIDS</li> <li>• Interstitial lung disease</li> </ul>
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- Rib fracture or flail chest with leakage of air
- Fractures of paranasal sinuses
- Perforation of a hollow viscus, e.g. oesophagus or larynx (spontaneous or procedural)
- Gas gangrene

Always look for subcutaneous emphysema in a case of pneumothorax by palpation with pressure of fingers over the side involved. There will be palpable crepitus on finger pressure.

### 58. How will you investigate a patient with pneumothorax?

**Ans.** Investigations are done for sake of diagnosis and to find out the cause.

1. *Chest X-ray (PA view, Fig. 1.4B)* should be done first of all before any other investigation in case of suspected pneumothorax. It is done in erect position, sometimes expiratory film is taken especially in small pneumothorax. The radiological features are;
  - Increased translucency of the lung on the side involved with absence of peripheral lung markings.
  - The underlying lung is collapsed which is separated from airless peripheral translucent shadow (pneumothorax) by a pencil – sharp border.
  - Mediastinum is shifted to opposite side
  - Costophrenic angle is clear
  - Underlying lung disease may be apparent such as a tubercular cavity.

2. *Routine blood tests*, e.g. TLC, DLC, ESR, (raised ESR with relative mononuclear leucocytosis suggest tubercular aetiology).
3. *Montaux test* may be positive in tuberculosis
4. *Sputum for AFB* (3 consecutive specimens)
5. *Pulmonary function tests* (FEV<sub>1</sub>, FEV<sub>1</sub>/VC ratio, PFR etc. for COPD).

### 59. What are similarities and dissimilarities between pleural effusion and pneumothorax?

**Ans.** Similarities and dissimilarities are as follows:

- Some clinical features on chest examination whether there is air or fluid in the pleural space are similar due to shift of the mediastinum to opposite side and collapse of the underlying lung as a result of positive intrapleural pressure (normally there is negative pressure in the pleural space on both sides which keeps the mediastinum in the centre). The similarity of signs include diminished movements and expansion, fullness of intercostal spaces on the side involved, shift of mediastinum to opposite side, hyperactivity of extra-respiratory muscles, diminished or bronchial breath sounds and decreased or increased vocal resonance with no added sounds.
- The dissimilarities include hyper-resonant note on percussion in pneumothorax with obliteration or masking of liver dullness in right-sided pneumothorax and splenic dullness on left side pneumothorax. In pleural effusion, the percussion note is stony-dull on the side and over the part involved. The dullness is continuous with liver dullness on right side and cardiac dullness on left side with obliteration of resonance of Traube's area.

**Tip.** Absolute similarity is silent chest, i.e. no added sounds in both the conditions.

Absolute dissimilarity is hyper-resonant note in pneumothorax and stony dull in pleural effusion

**Note:** Bronchial breath sounds with increased vocal resonance can occur both in pleural effusion (at the upper level or apex) and bronchopleural fistula (open pneumothorax).

N.B. Questions regarding water-seal intercostal tube drainage, its indications, complications and reasons for non-expansion of the lungs after drainage have been discussed in instruments and procedures (Chapter 2).

## CASE 5: HYDROPNEUMOTHORAX

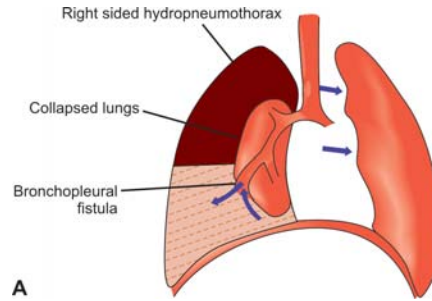
The patient whose X-ray is depicted as Figure 1.5B presented with fever, cough with expectoration, mucopurulent foul smelling without haemoptysis. The patient gave history of some abnormal sounds (crack-pots) on running or walking.

### Points to be Noted in the History

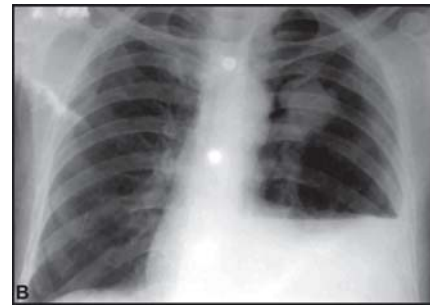
- History of fever or injury in the past.
- History of tuberculosis in the past
- Any history of pain chest, haemoptysis or a cardiac disorder.
- Any history of drainage of fluid in the past.

### General Physical Examination

- Patient is orthopnoeic, sitting in the bed
- Fever
- Tachypnoea, tachycardia
- Cyanosis
- Clubbing of fingers present in pyopneumothorax
- Accessory muscles of respiration may be active
- Shift of trachea and mediastinum to opposite side – *Sternomastoid sign* or *Trail sign* may be positive.



A



**Figs 1.5A and B: Hydropneumothorax:** A. Bronchopleural fistula with hydropneumothorax (right side); B. Chest X-ray (PA view) shows hydropneumothorax (left side)

### Clinical Presentation

- Dyspnoea at rest, cough
- Pain chest or heaviness in chest
- Splashing sound during jumping
- Fever, high grade with chills and rigors if pyopneumothorax

### Systemic Examination

#### Inspection

- Signs similar to open pneumothorax

#### Palpation

- Signs similar to open pneumothorax

#### Percussion

- A horizontal fluid level, above which percussion note is hyper-resonant and below which it is stony dull – hence, there is a clear cut transition between a hyperresonant to stony dull note
- Shifting dullness present because fluid has space (occupied by air) to shift
- Coin test is usually not positive.

#### Auscultation

- Succession splash present
- Amphoric bronchial breathing in bronchopleural fistula – a common cause of hydropneumothorax
- Tingling sounds heard

### 60. What is hydropneumothorax?

**Ans.** The presence of both air (above) and fluid (below) in pleural cavity is called *hydropneumothorax*. If instead of fluid, pus collects along with air, then it is called *pyopneumothorax*. Similarly collection of air and blood is called *haemopneumothorax*.

### 61. What are the differences between hydropneumothorax and pleural effusion?

**Ans.** Table 1.18 differentiates between hydropneumothorax and pleural effusion.

### 62. What are the causes of hydropneumothorax?

**Ans.** Common causes of hydropneumothorax are;

- Rupture of subpleural tubercular cavity (commonest cause)
- Rupture of lung abscess – actually it causes pyopneumothorax
- Penetrating chest injury with infection – again a cause of haemopneumothorax
- Acute pulmonary infarction (embolism)
- Following cardiac surgery
- *Iatrogenic*, i.e. introduction of the air during aspiration of pleural effusion
- *Pneumothorax*. Actually bronchopleural fistula (open pneumothorax) of tubercular aetiology is the commonest cause, but sympathetic collection of fluid



**Table 1.18:** Differentiating features of hydropneumothorax and pleural effusion

<i>Hydropneumothorax</i> (Fig. 1.5A)	<i>Pleural effusion</i>
<ul style="list-style-type: none"> <li>Shifting dullness on percussion present</li> <li>Horizontal fluid level, i.e. there is transition between hyper- resonant note (above) and stony dull note (below)</li> <li>Succussion splash present</li> <li>Tingling sounds especially after cough may be audible</li> <li>Coin-test sound in upper part of hydropneumothorax may occasionally be positive</li> <li>Diminished breath sounds and vocal resonance except in bronchopleural fistula where amphoric breath sounds may be heard</li> </ul>	<ul style="list-style-type: none"> <li>Shifting dullness absent (the rising dullness – Ellis S-shaped curve is now-a-days obsolete term)</li> <li>No such level</li> <li>No succussion splash</li> <li>No such sound</li> <li>Coin – test negative</li> <li>Sometimes, a tubular bronchial breathing with increased vocal resonance (bronchophony, whispering pectoriloquy and aegophony) present over the top of effusion</li> </ul>

in closed and tension pneumothorax may also lead to hydropneumothorax.

### 63. How will you explain absent shifting dullness, if present in a case of hydropneumothorax?

**Ans.** Hydropneumothorax contains air above (occupying a large space) and fluid below (occupying smaller space), both in moderate amount and are separated by a horizontal level (a line seen in peripheral lung field on chest X-ray, Fig. 1.5B)). Shifting dullness is present because fluid has space to shift by displacing air. Therefore, shifting dullness in hydropneumothorax will be absent if above mentioned conditions are not fulfilled.

- Loculated or encysted hydropneumothorax (both air and fluid are tightly packed)
- Too little air in hydropneumothorax
- Too much fluid in hydropneumothorax
- Thick viscid pus (sometime in pyopneumothorax).

### 64. What are the characteristic features of pyopneumothorax?

**Ans.** The patient will have all the clinical features of hydropneumothorax *plus*

- Presence of toxic look and prostration

- Hectic fever with chills and rigors
- Tachycardia, tachypnoea and clubbing of fingers
- Intercostal tenderness and tenderness during percussion (patient winces during percussion).

### 65. What are the differences between empyema thoracis and pyopneumothorax?

**Ans.** Clinical features of both empyema thoracis and pyopneumothorax are similar (hectic fever, signs of toxæmia, intercostal tenderness, diminished movements and diminished or absent breath sounds).

The differentiating features between the two are same as in case of pleural effusion versus hydropneumothorax such as presence of a horizontal level (transition between hyper- resonant and stony dull percussion note), shifting dullness, succussion splash in pyopneumothorax but not in case of empyema thoracis. However, it will be difficult to differentiate a loculated pyopneumothorax from empyema thoracis because of absence of above mentioned features.

### 66. How will you differentiate between a lung abscess and pyopneumothorax?

**Ans.** Table 1.19 differentiates between lung abscess and pyopneumothorax.

**Table 1.19:** Differentiating features between pyopneumothorax and lung abscess

<i>Pyopneumothorax</i>	<i>Lung abscess</i>
<ul style="list-style-type: none"> <li>Cough and expectoration minimal</li> <li>Shift of the mediastinum and trachea to opposite side</li> <li>Added sounds are absent</li> <li>Chest X-ray will show horizontal level starting from the periphery</li> <li>Vocal fremitus, breath sounds and vocal resonance diminished or absent</li> </ul>	<ul style="list-style-type: none"> <li>Copious purulent expectoration is a predominant feature</li> <li>No shift of trachea or mediastinum</li> <li>Added sounds such as crackles will be present</li> <li>A horizontal fluid level does not touch the periphery of the lung</li> <li>Vocal fremitus and vocal resonance may be decreased (cavity full of pus) or increased if lung abscess is empty and superficially placed. There can be a bronchial breathing as heard over a cavity</li> </ul>

### 67. How will you investigate a patient with pyopneumothorax?

**Ans.** Investigations are as follows:

1. *Routine blood tests* such as TLC, DLC and ESR for leucocytosis as an evidence of infection
2. *Sputum examination* for culture and sensitivity
3. *Chest X-ray (PA view)* will show;
  - A horizontal fluid level
  - Increased radiolucency above the horizontal level without lung markings with a homogeneous opacity below the horizontal level (Fig. 1.5B)
  - Shifting of trachea and mediastinum to the opposite side

X-ray should be taken in upright position to show a fluid level

- The collapsed lung due to compression from outside is usually hidden within homogeneous opacity of fluid and may not be visible on X-ray.

4. *Aspiration of fluid* or the thick exudate (pus) will be done which is sent for culture and sensitivity.

**68. Name the diagnostic signs of hydropneumothorax/pyopneumothorax. How will you elicit them?**

Ans. Diagnostic signs are as follows:

1. A horizontal level, i.e. upper part of hydropneumothorax is hyper-resonant due to presence of air and lower part is dull due to presence of fluid/pus
2. Shifting dullness
3. Succussion splash
4. Tingling sounds on auscultation.

To elicit these signs, Read Clinical Methods in Medicine by SN Chugh.



## CASE 6: COLLAPSE OF THE LUNG

The patient whose X-ray (Fig. 1.6A) is depicted presented with cough, dry hacking without haemoptysis and acute breathlessness.

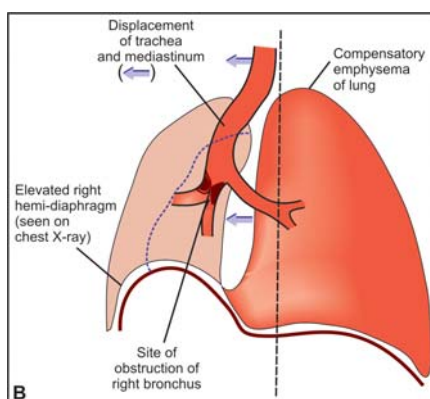
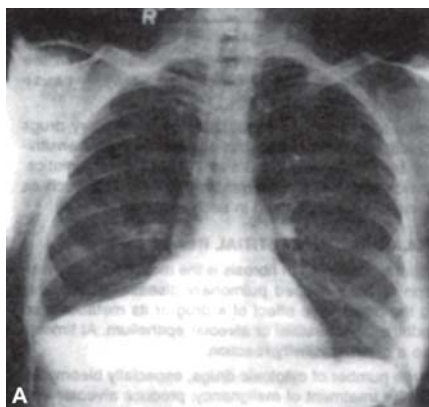
## Points to be Noted in the History

- Past history of tuberculosis or malignancy
- Any history of swelling in the neck, axilla or groin
- Past history of mumps, measles and whooping cough during childhood
- Past history of rheumatic heart disease or pericardial disease (fever, chest pain).

## General Physical Examination

Look for the followings;

- Patient may dyspnoeic, orthopnoeic if major bronchus is involved
- Central cyanosis
- Tachypnoea, tachycardia
- Fever  $\pm$  (develops in fibrosing alveolitis or in bronchogenic carcinoma)



**Figs 1.6A and B:** A. Chest X-ray showing collapse of right upper lobe; B. Diagrammatic illustration of collapse lung

## Clinical Presentations

- Pain on the affected side
- Breathlessness
- Dry cough and fever

Presence of symptoms depends on;

- Rapidity with which they develop
- Amount of the lung involved
- Presence or absence of infection

## Systemic Examination

## Inspection

- Flattening or depression of the chest on affected side
- Crowding of the ribs and narrowing of intercostal spaces
- Diminished movements on the side involved
- Shifting of trachea, apex beat towards the side involved (pulling effect) – Trail's sign
- Kyphoscoliosis may result in long-standing collapsed lung with fibrosis
- Drooping of shoulder if apex of the lung is collapsed

## Palpation

- Shifting of trachea and mediastinum to the same side
- Reduced movements of the chest on involved side
- Reduced expansion of the chest on side involved
- Vocal fremitus on the affected side may be;
  - Diminished or absent if bronchus is totally occluded
  - Increased if bronchus is patent.

## Percussion

- Impaired or dull note on the side affected

## Auscultation

## Collapse with obstructed bronchus

- Diminished or absent breath sounds
- Diminished/absent vocal resonance
- No added sounds

## Collapse with patent bronchus

- Tubular bronchial breath sounds
- Increased vocal resonance with bronchophony and whispering pectoriloquy
- Coarse crackles may be heard occasionally

### 69. What do you understand by the term collapse of the lung?

**Ans.** Pulmonary collapse or atelectasis is defined as “airlessness with shrinkage” of a part or the whole lung. Atelectasis may be present since birth (*atelectasis neonatorum*) due to failure of the lung to expand, or may occur anytime during life (acquired atelectasis) due to absorption of air secondary to obstruction, compression, contraction or surfactant loss.

### 70. What are various types of collapse?

**Ans.** Localised/ hemithoracic loss of lung volume (collapse of the lung) can occur with patent bronchus or with occluded bronchus (obstructive collapse) or there is compression of the lung from outside (intrapleural positive pressure), hence, it is of two main types;

1. Obstructive collapse (absorption or resorption collapse, Fig. 1.6B). It occurs due to absorption of air distal to obstruction in the alveoli. The site of obstruction can be central or peripheral.
  - i. Central obstructive collapse is with obstructed major bronchus
  - ii. Peripheral obstructive (absorption) collapse is always with patent surrounding bronchus.
2. *Compression collapse (Relaxation collapse)*. It occurs from relaxation of the lung due to pleural disease (e.g. pleural effusion, pneumothorax and hydropneumothorax).

### 71. What are the causes of collapse of the lung?

**Ans.**

#### 1. Obstructive (absorption collapse)

A. *Central (major bronchus)* The causes are;

Common	Rare
<ul style="list-style-type: none"> <li>• Bronchial adenoma or carcinoma</li> <li>• Enlarged tracheobronchial lymph nodes (malignant, tubercular)</li> <li>• Inhaled foreign body, Misplaced endotracheal tube</li> <li>• Mucus plugging</li> </ul>	<ul style="list-style-type: none"> <li>• Aortic aneurysm</li> <li>• Giant left atrium</li> <li>• Congenital bronchial atresia</li> <li>• Stricture/stenosis</li> <li>• Pericardial effusion</li> </ul>

B. *Peripheral (divisions of bronchus/bronchi)*

- Pneumonias
- Mucus plugging (sputum retention)

- Asthma
- Pulmonary eosinophilia

#### 2. Compression collapse (relaxation collapse)

- Pleural effusion
- Pneumothorax
- Hydropneumothorax, pyopneumothorax, hemopneumothorax.

### 72. What are the clinical differences between central obstructive and peripheral obstructive collapse?

**Ans.** Remember that peripheral collapse does not involve the major bronchus, involves divisions of bronchus or bronchi with the result the collapse occurs with patent bronchus (i.e. surrounding bronchi are patent) while, central obstruction of a major bronchus leads to collapse of all its divisions, hence, the whole lobe is airless with no patent bronchus. The differentiating features are summarised in Table 1.20. The causes of both types of obstructive bronchus are given above.

Signs of compression collapse means signs of pleural effusion/pneumothorax. The underlying collapsed lung is silent (relaxed hence called relaxation collapse). In this type of collapse, trachea and mediastinum is shifted to the opposite side due to pushing effect of fluid/air.

### 73. What are the clinical pulmonary presentations of bronchogenic carcinoma?

**Ans.** Clinical pulmonary presentations of bronchogenic carcinoma are;

- Collapse
- Cavitation
- Mediastinal compression/obstruction-superior vena cava syndrome
- Pancoast's tumour- Apical carcinoma may involve brachial plexus producing monoplegia
- Consolidation—a solid tumour
- Pleural effusion—rapid filling, haemorrhagic.

### 74. How will you investigate a patient with lobar collapse?

**Ans.** Investigations of lobar collapse are;

- Routine blood examination
- Sputum examination – cytology, microbiology and culture

**Table 1.20:** Differentiative features of central obstructive and peripheral obstruction collapse of lung

Feature	Central obstructive collapse (occluded bronchus)	Peripheral obstructive collapse (patent bronchus)
• Shift of trachea and mediastinum	To the same side	To the same side
• Elevated dome of the diaphragm	On the same side	On the same side
• Breath sounds	Absent on the side involved	Tubular (bronchial) breath sounds
• Vocal resonance	Decreased/absent on the side involved	Increased vocal resonance with whispering pectoriloquy
• Common cause	• Tumour or lymph node or a foreign body	• Mucus plugging, ipsilateral bronchial cast or clot
• CT scan or chest X-ray	Collapse with loss of open bronchus sign— Golden's "S" sign	Collapse with open bronchus
• Signs on the other side	Signs of compensatory emphysema i.e. hyper-resonant note, vesicular breathing with prolonged expiration	No signs of compensatory emphysema on the other side

- *Chest X-ray (PA and lateral view)*. It will show;
  - Homogeneous opacity of the collapsed lung
  - Displacement of trachea and cardiac shadow (mediastinum) to the diseased (involved) side
  - Crowding of the ribs with reduction of intercostal spaces due to loss of volume of the lung on the side involved
  - Elevation of hemidiaphragm on the side involved
  - Pleural effusion on the side involved if collapse is due to malignancy of lung
  - Sometimes, the radiological features of underlying cause (hilar lymphadenopathy), foreign body may be evident
- *CT scan* to find out the cause
- *Bronchoscopy* to find out the cause and to take biopsy
- *Scalene node biopsy*, if lymph node enlarged or malignancy lung suspected
- *Pleural fluid examination* if pleural effusion present.

*Note:* Investigations of compression collapse are same as that of pleural effusion.

### 75. What are the differences between collapse of the lung and localised fibrosis?

**Ans.** Table 1.21 differentiates between collapse and fibrosis.

**Table 1.21:** Differentiating features of lung collapse and fibrosis

Feature	Collapse	Fibrosis
Onset	Acute	Chronic
Chest wall	Flattened	Retracted
Breath sounds	Absent	Feeble but never absent

### 76. What are the complications of collapse?

**Ans.** Common complications of collapse are:

- Secondary infection
- Spontaneous pneumothorax from ruptured bullae of compensatory emphysema on the uninvolved side of the lung.

## CASE 7: DIFFUSE FIBROSING ALVEOLITIS

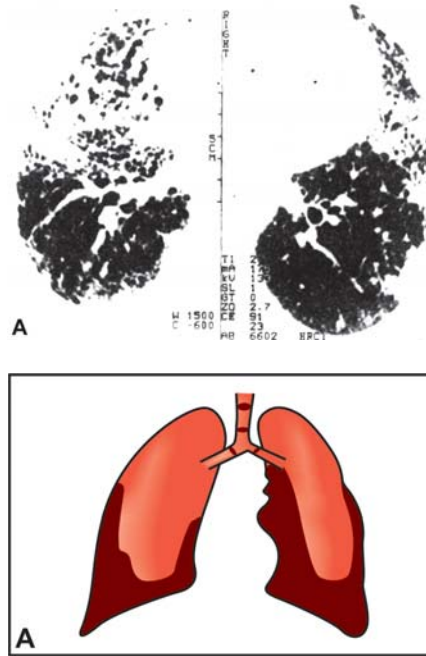
The patient (i.e. a coal-mine worker) whose CT scan is depicted as Figure 1.7A presented with progressive dyspnoea and cough for the last 2 years. The dyspnoea was exertional in the beginning, increased to occur now at rest. There was history of associated fever, weight loss, malaise and fatigue.

### Points to be Noted in the History

- Past history of tuberculosis or lung suppuration
- Any history of radiation exposure
- Any history of joint pain, arthralgia, rash
- Drug history
- Occupational history, e.g. coal miner, stone cutter, farmer or industrial worker
- Past history of rheumatic heart disease or any other cardiac disorders.

### General Physical Examination

- Dyspnoea, orthopnoea
- Tachypnoea
- Central cyanosis (if severe)
- Clubbing of the fingers
- Signs of occupation
- Raised JVP and ankle oedema if severe disease



**Figs 1.7A and B:** A. CT scan chest showing honey-comb appearance in a patient with diffuse fibrosing alveolitis, B. Diagrammatic illustration

### Clinical Presentation

- Progressive exertional dyspnoea
- Persistent dry cough
- Fever, weight loss, fatigue
- At the late stages, patient may complain of symptoms of cor pulmonale (abdominal pain due to hepatomegaly, ascites, swelling legs)

### Systemic Examination

#### Inspection

- Increased respiratory rate
- Bilateral symmetrical reduction in chest movements
- Accessory muscles of respiration may be hyperactive

#### Palpation

- Reduced bilateral chest movements
- Reduced expansion of the chest
- Bilateral reduction of vocal fremitus

#### Percussion

- Dullness on percussion at lung bases on both sides

#### Auscultation

- Bilateral crackles (end- inspiratory) at both the bases (lower zones) of the lungs
- Vesicular breathing diminished in intensity
- Vocal resonance bilaterally diminished

#### Other system examination

- Signs of right heart failure (raised JVP, hepatomegaly, central cyanosis and pitting oedema)

### 77. What is your clinical diagnosis?

**Ans.** The patient being an occupational workers (coal-miner), developed symptoms of progressive dyspnoea and cough, fever and weight loss, the probable diagnosis will be occupational lung disease (e.g. coal-miner pneumoconiosis).

### 78. What do you understand by fibrosis of the lung? What are its causes?

**Ans.** Fibrosis of the lung means replacement of lung parenchyma by fibrous tissue. It occurs usually as a reactive process or a healing /reparative process.

### Causes

1. *Focal fibrosis*
  - Pneumoconiosis
2. *Reparative fibrosis /replacement fibrosis*
  - Tuberculosis
  - Following bronchiectasis, lung abscess, pulmonary infarction
  - Following radiation
3. *Interstitial fibrosis (it is bilateral fibrosis of alveolar walls and septa)*

### A. Pulmonary origin

- *Hypersensitivity*
  - Diffuse fibrosing alveolitis (Fig. 1.7B)
  - Farmer's lung
- *Collagen vascular disorders*
  - SLE
  - Systemic sclerosis
  - Rheumatoid arthritis (rheumatoid lung)
- Lymphangitis carcinomatosa
- Drug-induced, e.g. busulphan, bleomycin, nitrofurantoin, methysergide, hydralazine, hexamethonium
- *Miscellaneous*
  - Sarcoidosis
  - Aspiration pneumonitis
  - Histiocytosis
  - Tuberous sclerosis
  - Xanthomatosis

### B. Cardiac origin

- Multiple pulmonary infarcts
- Mitral stenosis

### C. Idiopathic

- Hamman-Rich disease.

### 79. What is Hamman-Rich syndrome? What are its clinical features?

**Ans.** Diffuse interstitial fibrosis or fibrosing alveolitis of acute onset, progressive course of unknown aetiology is called *Hamman-Rich syndrome*. It is characterised by progressive dyspnoea, dry cough, fever, weight loss and signs of bilateral fibrosis of the lung.

The clinical characteristics (physical signs) have already been described in the beginning.

### 80. How will you investigate a patient with cryptogenic fibrosing alveolitis?

**Ans.** The common investigations are as follows:

1. *Routine blood tests*
2. *Blood for rheumatoid factor and antinuclear antibodies*
3. *Chest X-ray (PA view) shows;*
  - Diffuse pulmonary opacities in the lower zones peripherally.
  - The hemidiaphragm are high and the lungs appear small

- In advanced disease, there may be "honey-comb" appearance of the lungs in which diffuse pulmonary shadowing is interspersed with small cystic translucencies.

4. *High resolution CT scan* may show honey-combing and scarring, most marked peripherally in both the lungs. CT scan is useful in early diagnosis when chest X-ray may not show the radiological changes.
5. *Pulmonary function tests.* There is restrictive ventilatory defect with reduction in FEV<sub>1</sub> and vital capacity (VC). The carbon monoxide transfer factor is low and lung volumes are reduced (Read pulmonary function tests in the beginning of this chapter – Table 1.5).
6. *Bronchoalveolar lavage and transbronchial biopsy* may sometimes be helpful
7. *Open lung biopsy* for histological patterns of idiopathic cases of interstitial lung disease.

### 81. What is respiratory bronchiolitis?

**Ans.** Respiratory bronchiolitis is an interstitial lung disease of smokers in which there is accumulation of pigment-laden macrophages in the respiratory bronchioles and adjacent alveoli leading to mononuclear cell infiltration and fibrosis. It may reverse on cessation of smoking.

Clinical picture is similar to cryptogenic fibrosing alveolitis.

### 82. What is farmer's lung?

**Ans.** It is an occupational lung disease caused by an inhalation of organic dust (mouldy hay, straw, grain), characterised by features of extrinsic allergic alveolitis (e.g. headache, muscle pains, malaise, pyrexia, dry cough and breathlessness without wheeze) which may progress to irreversible pulmonary fibrosis.

The pathogenic mechanism is local immune response to fungal antigen, e.g. micropolyspora faenae or aspergillus fumigatus.

The diagnosis is based on; (i) clinical features, (ii) characteristic radiological features as described above, (iii) high-resolution CT scan and (iv) identification of potential antigen by ELISA or precipitin antibody test.

The treatment is removal of the source of antigen wherever possible and a course of 3-4 week of prednisolone (40 mg/day) may arrest the process.



**83. What is coal-worker's pneumoconiosis?**

**Ans.** The disease follows prolonged inhalation of coal dust hence, is an occupational lung disease seen in coal-workers. The condition is subdivided into *simple pneumoconiosis* and *progressive massive fibrosis* for both clinical purposes and certification.

**The simple coal miner's pneumoconiosis** is reversible (it does not progress if miner leaves the industry), non-progressive and radiologically characterised by nodulation without cavitation. On the other hand, progressive massive fibrosis – a variety of coal miner's pneumoconiosis is irreversible, progressive and radiologically characterised by large dense masses, single or multiple, occur mainly in upper lobes associated with cavitation. Tuberculosis may be a complication. It carries poor prognosis.

**84. What is Caplan's Syndrome?**

**Ans.** It consists of association of rheumatoid arthritis (positive rheumatoid factor) in patients with coal worker's pneumoconiosis with rounded fibrotic nodules (nodular

shadowing) 0.5 to 5 cm in diameter distributed mainly in the periphery of the lung field.

Caplan's syndrome—Rheumatoid arthritis plus coal-worker's pneumoconiosis.

**85. What is Silicosis?**

**Ans.** This disease is caused by inhalation of silica dust or quartz particles, characterised by progressive development of hard nodules which coalesce as the disease progresses followed by fibrosis. The clinical and radiological features are similar to coal worker's pneumoconiosis though changes tend to be more marked in the upper lobe. The hilar shadow may be enlarged; *egg-shell* calcification in the hilar lymph node is a distinct feature. Tuberculosis may be a complication and may modify the silicotic process with ensuring caseation and calcification. The disease progresses even when the exposure to dust ceases.

**86. What is asbestosis? What are its possible effects on respiratory tract?**

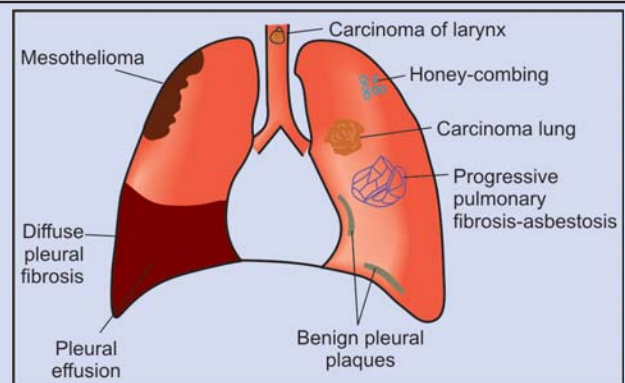
**Ans.** Table 1.22 explains features of asbestosis and its side effects on respiratory tract.

**Table 1.22:** Features of asbestosis

*Asbestosis* is an occupational lung disorder, occurs due to exposure to fibrous mineral asbestos in certain occupations such as in the mining and milling of the mineral. The main types of mineral asbestos involved in asbestosis are;

- *Chrysotile* (white asbestos – a common factor)
- *Crocidolite* (blue asbestos – uncommon factor)
- *Amosite* (brown) asbestos –a rare factor)

The possible effects of asbestosis are depicted in Figure 1.7C.



**Fig. 1.7C:** Asbestos; its possible effects on the respiratory tract

## CASE 8 CAVITY WITH FIBROSIS

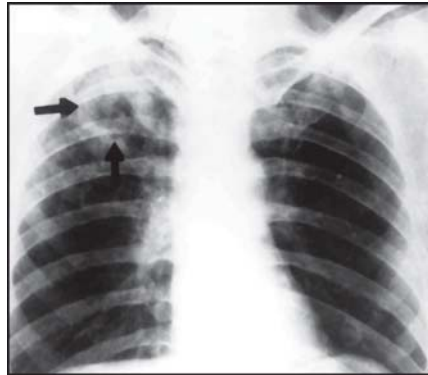
The young patient whose X-ray is depicted (Fig. 1.8A) presented with cough, fever, haemoptysis and weight loss for the last 6 months. There was history of weakness and decreased appetite and night sweats.

## Points to be Noted in the History

- Onset and progression of the symptoms
- Past history of tuberculosis or malignancy
- Past history of pneumonia (e.g. fever, cough, haemoptysis and pain chest) or lung suppuration (cough with mucopurulent or purulent sputum)
- Any history of headache, vomiting, visual disturbance or neurological deficit.

## General Physical Examination

- Patient may be ill-looking, emaciated
- Repeated coughing and bringing out a large amount of sputum
- Tachypnoea and tachycardia
- Fever
- Clubbing of fingers and toes
- Weight loss
- Oedema feet if secondary amyloidosis develops and involves the kidneys



**Fig. 1.8A:** Chest X-ray (PA view) showing a cavity with fibrosis

## Clinical Presentations

- Cough, fever and night sweats, weakness may be initial manifestations of *tubercular cavity*
- Cough, massive expectoration, fever, purulent sputum with postural and diurnal variation suggest *lung abscess* or *bronchiectasis*
- Cough, haemoptysis, breathlessness, fever, weight loss, anorexia suggest *malignancy* as the cause of cavity.

## Systemic Examination

## Inspection

- Diminished movement on the side involved (right side in this case)

## Palpation

- Movements of the chest reduced on the side involved (right side in this case)
- Expansion of the chest is reduced if cavity is large
- Shift of trachea and mediastinum to the same side if there is a large cavity with fibrosis (right side in this case)

## Percussion

- Dull percussion note over the cavity. Rest of the lung is normally resonant

## Auscultation

- Amphoric or cavernous bronchial breathing over the cavity
- Increased vocal resonance over the area of cavity with bronchophony
- Mid-inspiratory and expiratory crackles
- Post-tussive crackles
- Crackpot sounds

Note: All the above mentioned signs will be present only if the cavity is large, superficial and communicates with bronchus. Deep seated cavity may not produce any physical sign.

## 87. What is your clinical diagnosis?

**Ans.** In view of history of cough, fever, haemoptysis of 6 months duration and signs of cavitation in this patient suggest either a tubercular or a malignant cavity in the lung.

## 88. What do you understand by the term “cavity”?

**Ans.** Pulmonary cavity is an area of liquefaction necrosis within the lung parenchyma in communication with a patent bronchus. The cavity may be empty or may be filled with secretions and infected material.

*Pseudocavity* means appearance of a cavity on chest X-ray which may be obtained with summation of shadows of vessels, ribs and calcification.

## 89. What are causes of cavitation in the lung?

**Ans.** Common causes are:

## 1. Infection

- Tuberculosis
- Lung abscess
- Bronchiectasis
- Fungal infection
- Ruptured hydatid cyst with infection

2. *Congenital*
  - Infected bronchogenic cyst
  - Sequestration
  - Polycystic lungs
3. *Neoplasm*
  - Bronchogenic carcinoma
  - Metastasis
  - Lymphoma
4. *Trauma*
  - Resolving haematoma
5. *Immunological*
  - Rheumatoid arthritis
  - Wegener's granulomatosis
6. *Vascular*
  - Pulmonary infarction
7. *Infected emphysematous bullae.*

**90. What are the various types of cavity seen in the lung?**

**Ans.** Types of cavities are as follows:

1. *Thin-walled* A cavity is surrounded by a thin walled margin of lung tissue. The margin may be irregular, shaggy in lung abscess (*staphylococcal*) and bronchogenic carcinoma while it is smooth and regular in tuberculosis, lung cyst, emphysematous bullae, hydatid cyst and fungal infection.
2. *Thickened walled* A thick wall is formed by thick exudative material or heaps of cells such as in lung abscess, tuberculosis and bronchogenic carcinoma.

**91. What are the physical signs of a cavity?**

**Ans.** Typically, a superficial large cavity communicating with the bronchus produces signs which depend on whether the cavity is empty or filled with fluid at the time of examination. The signs of cavity are given in Table 1.23.

**92. What is amphoric breath sounds? What are its causes?**

**Ans.** Read clinical methods by Prof. S.N. Chugh.

**93. What type of bronchial breathing occur over a cavity?**

**Ans.**

- Thin walled cavity with narrow bronchus produces amphoric bronchial breathing
- Thick walled cavity with patent (narrow or wide) bronchus produces cavernous breathing.

**Table 1.23:** Physical signs over a cavity

Sign	Empty	Filled
• Movement of chest on the side and area involved	Diminished	Diminished
• Retraction/flattening of chest	Present	Present
• Tactile vocal fremitus and vocal resonance	Increased	Decreased
• Percussion note	Crackpot sound	Diminished
• Breath sounds	Amphoric/cavernous	Diminished
• Whispering pectoriloquy	Present	Absent
• Post-tussive crackles/rales	Absent	Present

**94. What are its complications of a tubercular cavity?**

**Ans.**

- A source of intercurrent infections
- Meningitis (tubercular) or miliary tuberculosis
- Secondary amyloidosis in case of long-standing cavity
- Hydropneumothorax.
- Chronic cavity may lead to malnutrition or hypo-proteinaemia

**95. What do understand by the term lung abscess? What are its causes?**

**Ans.** *Definition* It is defined as collection of purulent material in a localised necrotic area of the lung parenchyma. It is a suppurative lung disease.

*Causes* Most of the lung abscesses are pyogenic in origin, but, sometimes it may be nonpyogenic such as necrosis in a tumour followed by cavitation and collection of material. This is called *malignant lung abscess*. The causes of the abscesses are given in Table 1.24.

**96. What are its clinical features?**

**Ans.** Clinical presentations and examinations of lung abscess are given in Table 1.25.

**97. How will you investigate a case with lung abscess?**

**Ans.** The aims of investigations are:

- i. To localise the site of an abscess
- ii. To determine the underlying cause

**Table 1.24:** Causes of lung abscess

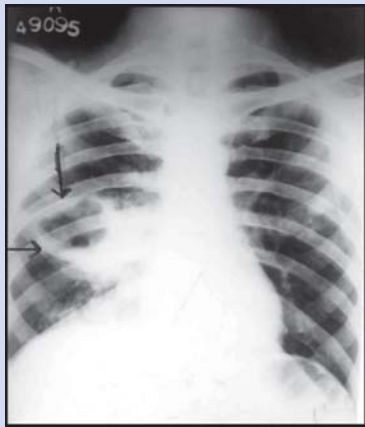
1. **Necrotising infection**
  - a. Pyogenic, e.g. *Staph. aureus*, *klebsiella*, group A *streptococci*, *bacterioides*, anaerobes, *nocardia*
  - b. *Tubercular* – a tubercular cavity with collection of purulent material
  - c. Fungi, e.g. *aspergillus*, *histoplasma*
  - d. Amoebic lung abscess secondary to liver abscess
2. **Embolic infarction with cavity formation**
  - Thromboembolism of the lung
  - Metastatic lung abscess
3. **Malignancy of the lung with cavitation**
  - Bronchogenic carcinoma with secondary degeneration and cavitation
  - Metastatic lung abscess
4. **Miscellaneous**
  - Infected congenital cysts
  - Coal miner's pneumoconiosis

- iii. To plan the treatment
- iv. To detect complications.

The tests done are;

- *Blood examination* for anaemia and leucocytosis. Raised ESR that suggests infection especially tuberculosis (markedly elevated).
- *Sputum examination* for isolation of the organisms (Gram's staining, Ziehl-Neelsen stain), for cytology including malignant cell; and culture and sensitivity.
- *Blood culture* to isolate the organism. It is mostly sterile.
- *Urine examination* for proteinuria, pus cells and casts. Albuminuria indicates secondary renal amyloidosis.

**Table 1.25:** Physical and systemic examinations of lung abscess

General physical examination		Systemic examination
<ul style="list-style-type: none"> <li>• Toxic look</li> <li>• Fever, sweating, tachycardia, tachypnoea</li> <li>• Poor nutrition</li> <li>• <math>\pm</math> cyanosis</li> <li>• Clubbing of the fingers present</li> <li>• Oedema of legs if secondary renal amyloidosis or hypoproteinaemia due to massive expectoration develops</li> <li>• Foul smelling (foetid) sputum and breath (halitosis)</li> <li>• Source of infection in upper respiratory tract, e.g. tonsillar or parapharyngeal abscess or throat sepsis may be evident</li> <li>• Cervical lymphadenopathy may be present</li> </ul>	 <p><b>Fig. 1.8B:</b> Chest X-ray PA view showing lung abscess on right side (↑)</p>	<ul style="list-style-type: none"> <li>• All the signs present in a cavity filled with secretion/ necrotic material will be present as discussed above</li> <li>• In case of rupture lung abscess, either the signs of empyema thoracis, or pyopneumothorax as discussed earlier will be present</li> <li>• In case of rupture amoebic liver abscess, there will be history of expectoration of anchovy sauce sputum with tender hepatomegaly</li> <li>• In case of malignancy, there will be marked weight loss, cachexia, haemoptysis with signs of collapse or consolidation. In addition, there may be features of metastatic spread to the mediastinal lymph nodes or evidence of compression of neighbouring structures</li> </ul>
<b>Clinical presentations</b> <ul style="list-style-type: none"> <li>• Fever, sweating, palpitations, tachypnoea</li> <li>• Copious purulent or mucopurulent sputum with diurnal (more in the morning) and postural (more in lying down than sitting position) relation</li> <li>• Haemoptysis</li> <li>• Pain chest due to pleuritis if pleura involved</li> <li>• May present with symptoms of underlying disease e.g. tuberculosis, amoebic liver abscess, malignancy lung</li> <li>• May present with complication e.g. meningitis, empyema thoracis</li> </ul>		

- Chest X-ray (PA view—Fig. 1.8B and lateral view) will show;
  - An area of consolidation with breakdown and translucency. The walls of the abscess may be outlined
  - The presence of a fluid level inside the translucent area confirms the diagnosis
  - Empyema, if develops, will be detected by radiological appearance of a pleural effusion (read radiological appearance of pleural effusion)

Lateral film will show the site of an abscess depending on the position of patient at the time of abscess formation (Table 1.26).

- *Bronchoscopic aspiration* for diagnosis. The aspirate is subjected to cytology, microbiology and culture
- *Aspiration of empyema* – if develops.

**98. What are the complications of a lung abscess?**

**Ans.** Common complications are:

**Table 1.26:** Localisation of lung abscess

1. Patient lying down position
  - A. Right lung (commonest site)
    - Posterior segment of upper and superior segment of lower lobe
2. Patient in upright position
  - Basal segments of both the lobes

*Note:* The lung abscess is more common on right side due to less obliquity of right bronchus

- Involvement of other lung (transbronchial spread)
- Septicaemia, toxæmia
- Meningitis, brain abscess
- Empyema and pyopneumothorax
- Secondary renal amyloidosis
- Massive haemoptysis
- Emaciation and hypoproteinaemia in long-standing cases.



## CASE 9: PULMONARY TUBERCULOSIS

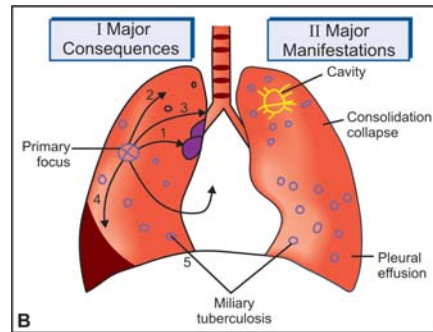
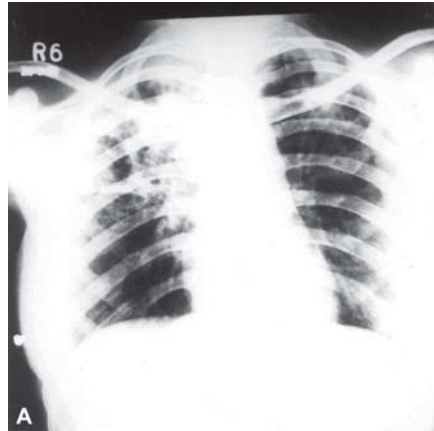
The patient whose X-ray is depicted (Fig. 1.9A) presented with cough, fever, haemoptysis, pain chest and weakness for the last 8 months. There was history of loss of weight, appetite and night sweats.

### History

- Write chief complaints in chronological order
- Note the onset and progression of the symptoms
- History of fever, cough, haemoptysis, breathlessness, pain chest/discomfort, any neurological deficit
- Any history of weight loss, decreased appetite right sweats or evening rise in temperature
- Ask complaints pertaining to other systems.

### General Physical Examination

- Ill-look
- Phlyctenular conjunctivitis
- Cervical or axillary lymphadenopathy
- Look for various sites for anaemia, jaundice cyanosis and oedema feet
- Look for JVP, trachea etc.
- Note any clubbing of the fingers
- Any joint involvement.



**Figs 1.9A and B:** Primary pulmonary tuberculosis. Consequences if left untreated are (Fig. 1.9A):

1. The primary focus may spread to hilar or mediastinal lymph node to form primary or Ghon's focus
2. Direct extension of primary focus into other part of lung
3. Extension of primary focus to bronchus
4. Extension of primary focus to pleura
5. Dissemination into blood stream leading to miliary tuberculosis

### Clinical Presentations (Fig. 1.9B)

Major manifestations

1. A cavity
2. Consolidation or collapse
3. Pleural effusion/empyema
4. Miliary tuberculosis
5. Hydropneumothorax or broncho-pleural fistula
6. Hilar lymphadenopathy
7. Bronchiectasis.

### Systemic Examination

#### Inspection

- Shape and symmetry of chest, Note any building or retraction.
- Look at the movements of chest at every quadrant of chest. Compare both sides with each other.
- Look at the apex beat e.g. location.
- Look for any distended veins or scar mark or mark for aspiration over the chest.
- Count the respiratory rate and note the type of breathing.
- Look for pulsations in supraclavicular fossa, epigastrium or other sites.

#### Palpation

- Palpate the apex beat to confirm its position.
- Palpate the trachea for any deviation.
- Note the expansion of the chest and measure it.
- Compare the vocal fremitus on both the sides.
- Palpate the intercostal space for any widening or narrowing.
- Palpate the crepitus or crackles or rub if any.

#### Percussion

- Percuss the lungs for resonance.
- Define cardiac and liver dullness.
- Percuss 2nd left and right intercostal spaces for dullness or resonance.
- Percuss directly the clavicles and supraclavicular areas for resonance.

#### Auscultation

- Hear the breath sounds and note the character and intensity and compare them on both the sides.
- Hear for any added sounds e.g. crackles, wheezes rub etc.
- Vocal resonance to be compared on both sides for increase or decreases.
- Elicit other specific signs depending on the underlying disease e.g. succession splash, coin test etc.

#### Other Systems

- Examine the spine for deformity and tenderness
- Examine abdomen for fluid or any organ enlargement
- Examine eyes for phlyctenular conjunctivitis or choroid tubercles.
- Elicit the signs of meningitis if suspected.

**99. What do you understand by the term primary pulmonary tuberculosis? How does it differ from post-primary tuberculosis?**

**Ans.** Infection with *M. tuberculosis* occurring most frequently through inhalation of infected droplets with the primary involvement of the lung is called primary pulmonary tuberculosis. Following inhalation, of *M. tuberculosis*, a subpleural lesion (*Ghon focus*) develops that causes rapid transport of bacilli to the regional (hilar) lymph nodes leading to development of primary complex (Table 1.27). The fate of the primary complex is as follows:

1. It may heal spontaneously within 1-2 months and *tuberculin skin test* becomes positive.
2. Spread of the primary focus to hilar and mediastinal lymph nodes to form primary complex which in most cases heals spontaneously.
3. It may remain dormant, becomes reactivated when the body defenses are lowered.
4. Direct extension of primary focus – called *progressive pulmonary tuberculosis* merging with post-primary TB.
5. Hematogenous spread leading to *miliary tuberculosis*, or *tubercular meningitis*.

**Table 1.27:** Primary focus

- Subpleural lesion (*Ghon focus*)
- Draining lymphatics from this focus to hilar lymph nodes
- Hilar lymphadenopathy

**Clinical Features of Primary Tuberculosis**

- Symptoms and signs of infection*, i.e. fever, influenza like illness, primary complex, skin test conversion.
- Symptoms and signs of the disease*, i.e. lymphadenopathy (hilar, paratracheal, mediastinal), collapse or consolidation (right middle lobe), obstructive emphysema, pleural effusion, endobronchial tuberculosis, miliary tuberculosis or, meningitis and pericarditis.
- Symptoms and signs of hypersensitivity*, e.g. erythema nodosum, phlyctenular conjunctivitis, dactylitis.

**Clinical Features of Post-primary Pulmonary Tuberculosis**

However, 85-90% of patients develop latent infection (positive tuberculin test or radiographic evidence of self-healed tuberculosis); and within this group 5-10% reactivate during their life-time resulting in post-primary disease, predominantly pulmonary (50% smear positive). Re-exposure to these smear – positive pulmonary tuberculosis may result in post-primary disease/ tuberculosis. The difference between progressive primary complex and post-primary tuberculosis are enlisted in Table 1.28.

**Table 1.28:** Differences between progressive primary and postprimary tuberculosis

Progressive primary complex	Post-primary tuberculosis
<b>Common in children</b>	<b>Common in adult</b>
1. Hilar lymphadenopathy	Absence of lymph node enlargement
2. Subpleural focus or focus in any part of the lung	Usually apical fibrosis
3. Cavitation rare	Cavitation common
4. Fibrosis uncommon	Fibrosis common
5. Miliary tuberculosis common	Miliary tuberculosis uncommon
6. Direct extension of primary focus	Re-exposure to smear positive pulmonary disease

**100. What are clinical presentations of post-primary pulmonary tuberculosis?**

**Ans.** Clinical presentations are as follows:

- Chronic cough, haemoptysis with signs and symptoms of a cavity or collapse/fibrosis
- Pyrexia of unknown origin (PUO)
- Unresolved pneumonia (consolidation)
- Pleural effusion
- Asymptomatic (diagnosed on chest X-ray)
- Weight loss, night sweats, evening rise of temperature, general debility (cryptic tuberculosis)
- Spontaneous pneumothorax.

**101. What is time table of tuberculosis?**

**Ans.** As already described, in 85-90% cases the primary complex heals spontaneous with or without calcification. In 10-15% cases, multiplication of tubercular bacilli is not contained and lymph nodes

enlargement results in either local pressure effects or lymphatic spread to the pleura or pericardium or rupture into adjacent bronchus or pulmonary blood vessel. The time table of tuberculosis is given in Table 1.29.

**Table 1.29:** Time table of tuberculosis

Time from infection	Manifestations
3-8 weeks	<ul style="list-style-type: none"> <li>Primary complex, positive tuberculin skin test, erythema nodosum</li> </ul>
3-6 months	<ul style="list-style-type: none"> <li>Collapse and bronchiectasis, adult pulmonary tuberculosis, miliary tuberculosis</li> </ul>
Within 1 year	<ul style="list-style-type: none"> <li>Pneumonia, pleural effusion</li> </ul>
Within 3 years	<ul style="list-style-type: none"> <li>Tuberculosis affecting bones, lymph node, joints, GI tract and genitourinary</li> </ul>
From 3 years onwards	<ul style="list-style-type: none"> <li>Post-primary disease due to reactivation or Reinfection</li> </ul>
Around 8 years	<ul style="list-style-type: none"> <li>Urinary tract disease</li> </ul>

### 102. What is cryptic tuberculosis? What is its presentation?

**Ans.** The term 'cryptic' means 'hidden'. A patient of tuberculosis with normal chest radiograph is called *cryptic tuberculosis*. Its presentation is as follows;

- Age over 60 years
- Intermittent low grade fever (PUO) with night sweats and evening rise
- Unexplained weight loss, general debility
- Hepatosplenomegaly (seen in 25% cases only)
- Normal chest X-ray
- Negative tuberculin skin test
- Leukaemoid reaction or pancytopenia
- Confirmation is done by biopsy (liver or bone marrow).

### 103. What are the stigmata of tuberculosis (evidence of present or past infection or disease)?

**Ans.** Stigmata attached with the tuberculosis are as follows:

- Phlyctenular conjunctivitis
- Erythema nodosum
- Tubercular lymphadenopathy with or without scars and sinuses
- Thickened, beaded spermatic cord
- Scrofuloderma
- Positive Mantoux test

- Localised gibbus, spinal deformity, paravertebral soft tissue swelling.

### 104. What are the chronic complication of pulmonary tuberculosis?

**Ans.** Common complications of pulmonary TB include;

#### 1. Pulmonary complications

- Massive haemoptysis
- Cor pulmonale
- Fibrosis/emphysema (compensatory)
- Recurrent infections
- Tubercular empyema
- Lung/pleural calcification
- Obstructive airway disease (endobronchial)
- Bronchiectasis
- Bronchopleural fistula

#### 2. Non-pulmonary complications

- Empyema necessitans
- Laryngitis
- Enteritis following ingestion of infected sputum
- Anorectal disease following ingestion of infected sputum
- Amyloidosis (secondary)
- Poncet's polyarthrititis

### 105. How will you investigate a case of pulmonary tuberculosis?

**Ans.** Investigations are as follows:

1. *Routine blood examination*, i.e. TLC, DLC, ESR for anaemia, leucocytosis. Raised ESR and C-reactive protein suggest tuberculosis.
2. *Montoux test* is non-specific (low sensitivity and specificity)
3. *Sputum* (induced by nebulised hypertonic saline, if not expectorated), or *gastric lavage* (mainly used for children) or *bronchoalveolar lavage* for acid-fast bacilli isolation (Ziehl-Neelsen stain) and culture.
4. *Chest X-ray* (AP, PA and lateral and lordotic views) for radiological manifestations of tuberculosis in the lungs. The varied manifestations are;
  - Soft fluffy shadow (confluent)
  - Apical infiltration
  - Dense nodular opacities.
  - Miliary mottling shadows (miliary tuberculosis)
  - A cavity or multiple cavities (irregular, thin walled)

- Fibrocaseous lesions
  - Tuberculoma
  - Calcification – lung and/or pleura
  - Bronchiectasis especially in the upper zones
  - Mediastinal (unilateral) lymphadenopathy (enlarged hilar lymph nodes)
  - Primary complex (Ghon focus) in children
5. *CT scan* for diagnosis and differential diagnosis
  6. *PCR (polymerase chain reaction)* with blood or any other fluid
  7. *ADA (adenosine deaminase)* levels increase in tuberculosis
  8. *Transbronchial biopsy*.

## CASE 10: BRONCHIAL ASTHMA

The patient (Fig. 1.10) presented with acute attack of breathlessness and cough. There was no history of pain chest or haemoptysis. There was history of such attacks in the past.

## Important Points to be noted in

## History

- Present history should cover the present symptoms in details.
- Past history should include any history of cough and cold in the childhood, chronic exposure to dust and smoke. Any history of recurrent attacks of nasal discharge and angioneurotic oedema.
- *Personal history* .e.g. smoking, alcohol, occupation, habits, diet
- *Family history* of bronchial asthma, hay fever and eczema

## General Physical Examination

- *Resting position* Patient is dyspnoeic and tachypnoeic during acute attack, sits in prop up position and uses extrathoracic muscles for respiration
- *Pulse* Tachycardia is usually present in acute attack. Marked tachycardia and bounding pulses indicate CO<sub>2</sub> narcosis (retention). Presence of *pulsus paradoxus* indicates severe acute asthma
- BP and temperature normal
- *Cyanosis* is present in severe acute asthma
- *Level of consciousness* Patients with mild attacks are fully conscious but anxious looking. Marked anxiety, drowsiness and restlessness indicate increasing severity of airway obstruction
- *Respiration*. Rate is more, respiration is rapid and shallow
- *Speech* If the patient can speak easily and in full sentences, the dyspnoea is mild. Monosyllabic speech suggests moderate dyspnoea. Inability to speak indicate severe asthma
- *Flapping tremors (asterixis)* on outstretched hands, papilloedema, and bounding pulses indicate CO<sub>2</sub> narcosis
- *Nasal examination* for polyp or allergic rhinitis. Throat examination for septic focus
- *Skin examination* for allergy



**Fig. 1.10:** A patient of acute severe asthma being nebulised

## Clinical Presentations

- Typical symptoms include wheeze, breathlessness, cough and tightness of chest. These symptoms may occur for the first time at any age and may be episodic or persistent.
- Episodic asthma presents with intermittent acute attacks, remains asymptomatic between attacks. The precipitating factor is either respiratory viral infection or exposure to allergens. This type of asthma occurs in children or young adults who are atopic.
- Persistent asthma presents with chronic wheezing and breathlessness, has to be differentiated from left heart failure (cardiac asthma). This is called adult onset asthma seen in older non-atopic individuals. Typically there is diurnal pattern in symptoms and PEF shows morning dipping. Cough and wheezing are nocturnal and disturb the sleep-hence called *nocturnal asthma*.

## Systemic Examination

## Inspection

*Patient is dyspnoeic at rest*

- Accessory muscles of respiration and alae nasi are working
- Respiratory rate is increased
- Audible wheezing
- Excavation of suprasternal notch and supraclavicular fossae may be present with recession of intercostal spaces during inspiration
- Shape of the chest normal, but there may be pigeon-shape chest in long standing childhood asthma
- Tracheal tug absent

## Palpation

- Trachea is central
- Apex beat may not be palpable due to overinflated lungs
- Movements of the chest are bilaterally and symmetrically decreased.
- Expansion of the chest on the *measurement* is reduced
- Vocal fremitus is reduced uniformly on both the sides
- Wheeze/rhonchi may be palpable

## Percussion

- Resonant note all over the chest
- Liver dullness intact at normal 5th intercostal space in right mid-clavicular line
- Normal cardiac dullness

## Auscultation

- Vesicular breathing with prolonged expiration present all over the chest
- Vocal resonance reduced uniformly all over the chest
- Polyphonic expiratory and inspiratory wheezes (rhonchi) are heard over the chest
- Coarse crackles at both the bases
- No pleural rub



**106. What do you understand by the term bronchial asthma?**

**Ans.** *Bronchial asthma* is defined as a disorder characterised by chronic airway inflammation and increased responsiveness of tracheobronchial tree to a variety of stimuli resulting in temporary narrowing of the air passages leading to symptoms of cough, wheeze, tightness of chest and dyspnoea. Airflow obstruction is transient and reversible with treatment. It is not a uniform disease but rather a dynamic clinical syndrome comprising of two common distinct pattern; (i) episodic asthma in which acute attacks are precipitated by allergens or infection by respiratory virus. These attacks are short-lived and patient in-between attacks is symptom-free. These attacks are common in children who are atopic hence, called *extrinsic asthma*. The other pattern (ii) is persistent form in which there is chronic wheeze and breathlessness, these cases resemble patients of COPD. These individuals are nonatopic, and asthma develops in old age – called *intrinsic asthma*.

**107. What are the difference between extrinsic and intrinsic asthma?**

**Ans.** Table 1.30 differentiates atopic and nonatopic asthma.

**108. What is acute severe asthma?**

**Ans.** This term has replaced the previous horrifying term *status asthmaticus*. It is defined as either an acute attack of prolonged asthma or paroxysmal attacks of acute asthma where there is no remission of attacks in-between and they are not controlled by conventional bronchodilators. It is a life – threatening emergency, needs proper diagnosis and urgent treatment. The diagnosis is suggested by;

- Acute dyspnoea, orthopnoea with wheeze, tachycardia, tachypnoea and perspiration.
- Central cyanosis
- Dry (unproductive) cough with mucoid expectoration
- Respiratory distress with hyperactivity of extra-respiratory muscles (accessory muscles of respiration)
- Pulsus paradoxus
- Diminished breath sounds due to reduced air entry and minimal or absence of high-pitched polyphonic rhonchi (wheezes)

**Table 1.30:** Differentiating features of extrinsic and intrinsic asthma

<i>Extrinsic asthma (atopic)</i>	<i>Intrinsic asthma (non-atopic)</i>
<ul style="list-style-type: none"> <li>• Episodic, sudden onset</li> <li>• Early onset or childhood asthma</li> <li>• More wheeze, less cough</li> <li>• Mostly seasonal</li> <li>• Attacks may occur at any time of the day or night</li> <li>• Diurnal pattern, e.g. symptoms and peak expiratory flow show morning dipping with subsequent recovery</li> <li>• Non-exercise induced attacks</li> <li>• Positive family history of an allergic disorder</li> <li>• Skin hypersensitivity tests positive</li> <li>• Sodium cromoglycate is most effective</li> </ul>	<ul style="list-style-type: none"> <li>Non-episodic, chronic or persistent</li> <li>Late onset or adult asthma</li> <li>More cough, less wheeze</li> <li>Mostly non-seasonal</li> <li>Mostly attacks occur at night (nocturnal)</li> <li>Non-diurnal pattern</li> <li>Exercise-induced attacks</li> <li>No family history</li> <li>Skin tests negative</li> <li>Not effective</li> </ul>

Silent chest is a characteristic feature of acute severe asthma and is an ominous sign

- PEFR (peak expiratory flow rate) is <50% of predicted or patient's best.

**109. What are the parameters of assessment of severity of asthma?**

**Ans.** The parameters of life-threatening asthma are;

1. *Bed side parameters of severity*
  - Pulse rate >110/min
  - Pulsus paradoxus
  - Tachypnoea (rapid shallow respiration)
  - Unable to speak in sentences
  - PEF <50% of predicted or <100 L/min
2. *Life-threatening parameters*
  - Cannot speak
  - Central cyanosis
  - Exhaustion, confusion, obtunded consciousness
  - Bradycardia
  - "Silent chest"
  - Uncontrolled PEF
3. *Investigative parameters of life-threatening asthma*
  - A normal (5-6 kPa) or high CO<sub>2</sub> tension

**Table 1.31:** Various allergans and other substances likely to provoke an attack of asthma

Allergan	Efficacy/propensity	Preventive measures
<b>1. More common</b>		
• Pollens	Low	• Try to avoid exposure to flowering vegetation
• House dust	Low/doubtful	• Keep bed room windows closed
		• Vacuum cleaning of the mattress daily
		• Shake out the blankets and bed sheets daily
		• Dust bed room thoroughly
• Animal dander	High	Avoid contact with animal pets, e.g. dogs, cats, horses, etc
• Feathers in pillows or quilts	High	Substitute foam pillows and terylene quilts
• Drugs	High	Avoid all preparations of relevant drugs
• Insect web	High	Do not allow the insect web to collect
<b>2. Less Common</b>		
• Food/food items	Low	Identify and eliminate them from diet
• Chemicals/pollutants	High	Avoid exposure to chemicals/pollutants and/or change of an occupation

- Severe hypoxaemia ( $< 8$  kPa) especially if being treated with  $O_2$
- A low pH or high ( $H^+$ ) i.e. acidosis

#### 110. What are various precipitating factors of asthma and how to avoid them?

**Ans.** It is a hard fact that certain allergens/ drugs can precipitate asthma in sensitised individual, their knowledge is essential so as to prevent the development of life-threatening situation. The allergans encountered at home or at work place are listed in the box along with preventive measures (Table 1.31).

#### 111. What is persistent rhonchus/wheeze? What are its causes?

**Ans.** A localised wheeze persisting in a localised area could be due to

- Bronchiostenosis
- Foreign body obstruction
- Bronchiol adenoma.

#### 112. What are precipitating factors for acute attack of asthma?

**Ans.** 1. Allergans (Read Table 1.31)

2. Pharmacological stimuli e.g. drugs such as;

- Asprin and NSAIDs
- Beta blockers
- Colouring agents e.g. tartrazine
- Sulfiting agents e.g. potassium metabisulfite, potassium and sodium bisulfite, sodium sulfite and  $SO_2$  which are used in food industries. Exhasure

usually follows ingestion of these compounds in food and beverages e.g. Salads, fresh fruit, potatoes, shellfish and wine.

3. Environmental and air pollutions.

- Ozone, nitrous dioxide and  $SO_2$
- Dust, fumes, pollens

4. **Occupational factors**

- Metal salts e.g. platinum, chrome, nickle
- Wood and vegetable dusts e.g. grain, flour, cast or bean, coffee beans, gum acacia etc.
- Drugs e.g. antibiotics, piperazine.
- Industrial chemicals and plastics e.g. dyes
- Biological enzymes e.g. laundry detergents and pancreatic enzymes
- Animal and insect dusts and secretions

5. **Infections** e.g. viral

6. Exercise

7. Emotional stress

#### 113. What is wheeze? What are its types? What are its causes?

**Ans.** Read Clinical methods of Prof. S.N. Chugh.

#### 114. What are the causes of recurrent bronchospasm?

**Ans.** • Bronchial asthma

- Carcinoid tumour
- Recurrent pulmonary embols
- Chronic bronchitis with acute exacerbation
- Recurrent LVF (cardiac asthma)

**115. How does bronchial asthma differ from chronic bronchitis?****Ans.** See the Table 1.32**Table 1.32:** Differences between bronchial asthma and chronic bronchitis

<i>Feature</i>	<i>Asthma</i>	<i>Chronic bronchitis</i>
<i>Onset</i>	<i>Acute</i>	<i>Slow, insidious</i>
Age	Childhood, adolescents and middle age	Usually middle age or old patients
Pathogenesis	Allergic	Allergic-inflammatory
H/o Smoking	Absent	Present
Family history	May be positive	Negative
H/o Allergy e.g. rhinitis, hay fever eczema	Present	Absent
Duration of symptoms	No fixed duration	At least of 2 yrs duration
Nature of symptoms and signs	Intermittent episodic	Persistent, acute exacerbation can occur
Seasonal variation	Present	Absent
Symptoms	Dyspnoea > cough	Cough > dyspnoea
Signs	Wheezes/rhonchi are more pronounced than crackles	Both wheezes and crackles are present
Sputum and blood eosinophilia	Common	Uncommon
Pulmonary function tests	Usually normal	Usually abnormal

**CASE 11: BRONCHIECTASIS**

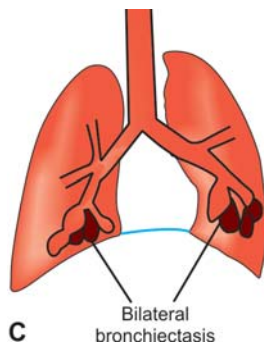
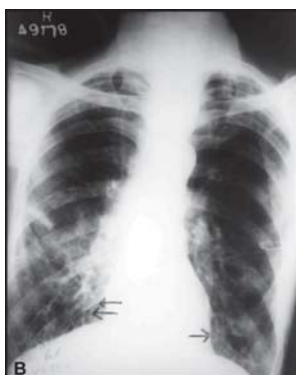
The patient (Fig. 1.11A) presented with history of cough with massive purulent (foul smelling) expectoration more than 250 ml a day with frequent streaking of the sputum with blood. The cough and expectoration was more in the morning in left lateral position.

**Points to be Noted in the History**

- Write the complaints in chronological order and detail them.
- Ask specifically about the amount of sputum, colour, consistency, smell etc.
- Is there any relationship between posture and cough?
- Past history of tuberculosis or childhood measles, mumps or whooping cough.
- Past history of recurrent fever or chest infection or asthma.
- Any history of oedema feet, swelling of the abdomen etc.
- Any history of fever, headache, vomiting, or neurological deficit.

**General Physical Examination**

- Patient may be dyspnoeic and has lots of coughing (coughing-coughing-coughing)
- Toxic look and fever if patient develops severe infection
- Pulse rate increased
- Respiratory rate may be high
- Nutrition may be poor due to hypoproteinaemia as a result of massive expectoration
- Cyanosis may be present, if disease is bilateral and severe or patient develops respiratory failure or cor pulmonale
- Clubbing of fingers and toes common; may be grade I to IV
- Oedema feet if there is cor pulmonale or hypoproteinaemia



**Figs 1.11A to C:** A. A patient with bronchiectasis bringing out massive mucoïd expectoration; B. X-ray chest; C. Diagram

**Clinical Presentations**

- Chronic cough, massive expectoration related to diurnal variation and posture
- Recurrent haemoptysis
- Recurrent pneumonias (fever, cough, pain chest due to pleurisy)
- Dyspnoea and wheezing
- Associated systemic symptoms, e.g. fever, weight loss, anaemia, weakness
- Oedema feet due to development of either cor pulmonale or involvement of kidney by secondary amyloidosis

**Systemic Examination***Inspection*

- The affected side of the chest may be retracted
- There may be diminished movement on the side involved
- There is wasting of muscles of thorax
- Look for the apex beat for dextrocardia.

*Palpation*

- Chest may be retracted with diminished movements and crowding of the ribs in the lower parts (s). There may be palpable wheeze or rhonchi and coarse mid-inspiratory and expiratory crackles.

*Percussion*

The percussion note is impaired over the area involved.

*Auscultation*

- Breath sounds may be bronchial, with coarse, bubbling leathery mid-inspiratory and expiratory crackles
- Vocal resonance may be increased

**N.B.** All the signs will be seen on both sides in bilateral disease.

**116. What do you understand by the term bronchiectasis?**

**Ans.** Bronchiectasis is a localised irreversible dilatation and distortion of bronchi. Although the definition is based on histopathological changes, yet clinical diagnosis is applied when chronic and recurrent infections occur in the dilated airways resulting in collection of secretions within them leading to massive expectoration, more so in the morning. It may be focal and unilateral (involvement of airway within limited region of the lung parenchyma) or diffuse and bilateral.

**117. What are its pathological types?**

**Ans.** Pathological types of bronchiectasis are:

1. *Cylindrical bronchiectasis*. The bronchi are uniformly dilated
2. *Varicose bronchiectasis*. The affected bronchi have irregular or beaded pattern of dilatation.
3. *Saccular (cystic) bronchiectasis*. The bronchi have ballooned or cystic appearance.

These pathological shapes can only be seen on bronchoscopy and CT scan.

**118. What are the causes of bronchiectasis?**

**Ans.** The causes of bronchiectasis are enlisted in Table 1.33. The most common cause is infection of bronchi with or without obstruction. Impaired pulmonary defense mechanisms such as immunoglobulin deficiency, cystic fibrosis may lead to bronchiectasis by repeated infections without obstruction. Some noninfective causes also lead to bronchiectasis.

**119. What is kartagener's syndrome?**

**Ans.** It consists of the following:

- Sinusitis
- Dextrocardia
- Bronchiectasis
- *Primary ciliary dyskinesia*. Because normal sperm motility also depends on proper ciliary function, males are generally infertile.

**120. What is dry or wet bronchiectasis?**

**Ans.** Chronic cough with massive purulent sputum, more in the morning and in one of the lateral or lying down position (postural relation depends on the side (s) involved), haemoptysis and dilated airways on the

**Table 1.33:** Causes of bronchiectasis

<b>1. Infective</b>
i. <i>Bacterial</i> , e.g. <i>P. aeruginosa</i> , <i>H. influenzae</i> , <i>S. aureus</i> , <i>Klebsiella</i> , <i>E. coli</i> , <i>B. proteus</i> , <i>M. tuberculosis</i> , mycoplasma, pertussis (a rare cause)
ii. <i>Viral</i> , e.g. measles, influenza virus, adenovirus, HIV
iii. <i>Fungal</i> – rare
<b>2. Obstructive</b>
• Endobronchial benign neoplasm (carcinoid tumour)
• COPD
• Foreign body aspiration leading to atelectasis and bronchiectasis in children
• Bronchiostenosis due to impacted secretions
• Extrinsic compression by enlarged lymph node
<b>3. Noninfective</b>
• Allergic bronchopulmonary aspergillosis
• Alpha-1 – antitrypsin deficiency
• Cystic fibrosis
• Kartagener's syndrome – primary ciliary dyskinesia leads to impaired bacterial clearance.

bronchoscopy or high resolution CT scan are characteristic features of *wet bronchiectasis*.

The term *dry bronchiectasis* refers to either asymptomatic disease or a disease with nonproductive cough associated with bronchiectasis in an upper lobe.

**121. How will you investigate a case of bronchiectasis?**

**Ans.** Following investigations are to be done:

- *Haemoglobin, TLC, DLC, ESR*. Polymorphonuclear leucocytosis with raised ESR suggest acute infection. There may be normocytic normochromic anaemia due to repeated infections.
- *Sputum for culture and sensitivity*. The sputum volume, colour, cellular elements are useful guide for active infection. Sputum for eosinophilia provides a clue to asthma and/or bronchopulmonary aspergillosis.
- *Urine examination* for proteinuria if amyloidosis is being suspected.
- *Blood culture and sensitivity* if there is evidence of bacteraemia or septicaemia
- *Chest X-ray (PA view)*. The chest X-ray (Fig. 1.11B) may be normal with mild disease or may show prominent (dilated) cystic spaces (saccular bronchiectasis) either with or without air-fluid levels, corresponding to the dilated airways. These dilated airways are often



crowded together in parallel, when seen longitudinally, appear as “tram-tracks”, and when seen in cross section appear as, “ring shadows”. These may be difficult to distinguish from enlarged airspaces due to bullous emphysema or from regions of honeycombing in patients with severe interstitial lung disease. Because these spaces may be filled with secretions, the lumen may appear dense rather than radiolucent, producing opaque tubular or branched tubular structures.

- *Bronchography* shows an excellent visualisation of bronchiectatic airways, but, now-a-days is not done because of availability of high resolution CT scan.
- *High resolution CT scan* will show dilated airways in one or both of the lower lobes or in an upper lobe. When seen in cross-section, the dilated airways have a ring like appearance.
- *Fibreoptic bronchoscopy*. It is done to find out the cause. When the bronchiectasis is focal, fibreoptic bronchoscopy may show an underlying endobronchial obstruction. Bronchiectasis of upper lobe is

common either due to tuberculosis or bronchopulmonary aspergillosis.

- *Pulmonary function tests*. These tests demonstrate airway obstruction as a consequence of diffuse bronchiectasis or associated COPD. Pulmonary function tests are useful to define the extent, severity of the disease, need for bronchodilators and to plan surgery.
- *Specific tests for aspergillosis* i.e. precipitin test and measurement of serum IgE.

### **122. What are the complications of bronchiectasis?**

**Ans.** Common complications are as follows:

- Recurrent pneumonias (e.g. repeated infections)
- Bacteraemia and septicaemia
- Massive haemoptysis (from dilated bronchial vessels) leading to pulmonary apoplexy
- Right ventricular failure or cor pulmonale
- Secondary amyloidosis
- Meningitis or brain abscess
- Aspergilloma (fungal ball) in a bronchiectatic cavity.

## CASE 12: JAUNDICE

The patient (Fig. 1.12) presented with fever for few days followed by jaundice and dark colouration of urine. There was history of pain abdomen, distaste to food.

### Pointed to be noted in History

A complete medical history is perhaps the most important part of evaluation. Ask for the following;

- Duration of jaundice
- Any change in appetite, taste, weight and bowel habits
- Any history of blood transfusions, IV injections, tattooing, unprotected sexual activity
- Recent travel history
- Exposure to people with jaundice either in the family, or locality or outside
- Exposure to possibly contaminated food
- Occupational exposure to hepatotoxins or chemicals
- Detailed drug history, i.e. taken in the past or are being taken. History of taking herbal or indigenous medicine
- History of alcohol intake
- History of pregnancy
- History of epistaxis, haematemesis or bleeding tendency
- Family history for congenital hyperbilirubinaemia, i.e. Gilbert's, Crigler-Najjar and Dubin-Johnson and Rotor syndromes
- Presence of any accompanying symptoms such as arthralgias, myalgias, weight loss, fever, pain in abdomen, pruritus and change in colour of stool or urine
- Symptoms of encephalopathy, i.e. mental features.

### General Physical Examination

- Assess the patient's nutritional status
- Look for stigmata of chronic liver disease. These are commonly seen in alcoholic cirrhosis.
  - Spider naevi
  - Palmar erythema
  - Gynaecomastia
  - Caput medusae
  - Dupuytren's contracture
  - Parotid glands enlargement
  - Testicular atrophy, axillary and pubic hair loss



**Fig. 1.12:** A patient with jaundice

### Clinical Presentations

The clinical presentation of a case with jaundice varies according to the cause.

1. Patients with hepatitis present with fever, abdominal pain, jaundice, tender hepatomegaly, anorexia, distaste to food and smoking.
2. Patients with haemolytic jaundice complain of insidious onset and long duration of jaundice with dark coloured urine and stools.
3. Patients with obstructive jaundice present with abdominal pain, pruritus and acholic stools in case the bile duct stone is the cause; while carcinoma of the pancreas produces painless progressive jaundice with palpable gall bladder.
4. Patient with cirrhosis of liver present with features of portal hypertension (ascites, haematemesis, malaena, splenomegaly) and jaundice develops during decompensation of liver disease, i.e. hepatic encephalopathy (mental features will be present)
5. Jaundice may present during each pregnancy in a patient with benign intrahepatic cholestatic jaundice of pregnancy.
6. A young patient with recurrent jaundice of long duration usually suffer from congenital hyperbilirubinaemia.

### Systemic Examination

#### Abdominal Examination for

- Hepatomegaly, e.g. note, size, shape, surface, movement with respiration, consistency and whether pulsatile or not. Elicit tenderness
- Splenomegaly—define its characteristics
- Ascites, elicit all the signs for detection of fluid
- Prominent venous collaterals or veins must be looked for. Determine the flow of blood
- Look at the hernial sites
- Look for scratch marks.

#### Other Systems Examination

- Cardiovascular, i.e. valvular heart disease, pericardial effusion

#### Respiratory System for

- Pleural effusion especially right-sided

#### Examination of excreta

- Urine
- Stool.

- Look for enlarged lymph nodes
  - An enlarged left supraclavicular node (Virchow's node) or periumbilical nodule (Sister Mary Joseph's nodule) suggests an abdominal malignancy
- JVP and other signs of right heart failure
- Look for pulse rate (bradycardia in obstructive jaundice), anaemia and scratch marks, Xanthelasma/xanthomatosis occur due to hypercholesterolaemia in obstructive jaundice.

### 123. How do you define jaundice? Where will you look for jaundice?

**Ans.** Jaundice or icterus refers to yellow discolouration of sclera, conjunctiva, mucous membrane of the tongue and skin due to raised serum bilirubin. Normal serum bilirubin is 0.3 to 1.5 mg%. Scleral staining or jaundice becomes clinically evident when serum bilirubin is at least 3.0 mg/dl. Raised bilirubin in between 1.5 and 3 mg/dl indicates subclinical jaundice.

#### Sites to be seen for Jaundice

Jaundice should be seen in sclera in broad day light because scleral icterus is difficult to examine in the presence of tube light or fluorescent light because of yellow reflection.

Jaundice first appears in sclera due to affinity of bilirubin to stain elastin in sclera. A second place to examine the jaundice is underneath tongue.

### 124. What are other causes of yellow discolouration of tissue?

**Ans.** Besides jaundice, other causes are;

- Carotenoderma (hypercarotenaemia) due to excessive consumption of fruits and vegetables rich in carotene (e.g. carrots, oranges, squash, peaches)
- Use of antimalarial drug, e.g. mepacrine, quinacrine
- Excessive exposure to phenols

Carotenoderma can be distinguished from jaundice by sparing of the sclera while it stains all other tissues. On the other hand, quinacrine stains the sclera

### 125. What are the causes of jaundice?

**Ans.** Jaundice reflects hyperbilirubinemia, indicates an imbalance between bilirubin production and clearance. Increased production and decreased clearance are the

underlying mechanisms for production of jaundice. Hyperbilirubinaemia may result from (i) overproduction of bilirubin, (ii) impaired uptake, conjugation or excretion of bilirubin, or (iii) regurgitation of unconjugated or conjugated bilirubin from damaged hepatocytes or bile ducts. *Unconjugated hyperbilirubinaemia* results from either overproduction or impaired uptake or conjugation of bilirubin. On the other hand, *conjugated hyperbilirubinaemia* is due to decreased excretion into the bile ductules or backward leakage of the pigment. The causes of jaundice are tabulated (Table 1.34).

### 126. How do you classify jaundice?

**Ans.** Jaundice is classified in different ways;

#### 1. Based on colouration of sclera

- *Medical jaundice* (yellow colouration)
- *Surgical jaundice* (greenish yellow colouration). The green colour is produced by oxidation of bilirubin to biliverdin in long- standing cases of jaundice.

#### 2. Based on the etiology

- *Haemolytic or prehepatic* (excessive destruction of RBCs)
- *Hepatic* (cause lies inside the liver)
- *Obstructive or posthepatic* (cause lies outside the liver in extrahepatic biliary system)

#### 3. Based on chemical nature of bilirubin

- *Unconjugated hyperbilirubinaemia*
- *Conjugated hyperbilirubinaemia* (conjugated bilirubin is  $\geq 50\%$  of total bilirubin. The normal conjugated bilirubin is just 15-20%)

### 127. What are characteristic features of hemolytic jaundice?

**Ans.** These are as follows;

**Table 1.34:** Causes of jaundice depending on the type of hyperbilirubinaemia**Jaundice with predominantly unconjugated hyperbilirubinaemia**

1. *Hemolysis* (excessive destruction of RBCs and/or ineffective erythropoiesis)
  - Intracorporeal or extracorporeal defects
  - Drug-induced especially in patients with G6PD deficiency
  - Infections, e.g. malaria, viral
  - Immune haemolysis
  - Microangiopathic haemolytic anaemia
  - Paroxysmal nocturnal haemoglobinuria
  - Ineffective erythropoiesis due to folate, v.t. B<sub>12</sub> and iron deficiency and thalassemia
2. *Decreased uptake of bilirubin*
  - Drugs, sepsis
  - Hepatitis (acute or chronic), decompensated cirrhosis
  - Gilbert's syndrome (congenital defect)
3. *Decreased conjugation of bilirubin*
  - Neonatal jaundice
  - Gilbert's and Crigler-Najjar syndrome – type I (complete absence) type-II (partial deficiency of enzyme glucuronyl transferase)

**Jaundice with predominantly conjugated hyperbilirubinaemia**

1. Cholestasis
  - A. *Intrahepatic*
    - Congenital (Dubin-Johnson and Rotor syndrome)
    - Benign intrahepatic cholestasis
    - Cholestatic jaundice of pregnancy
    - Drugs and alcohol
    - Hepatitis (acute and chronic)
    - Primary biliary cirrhosis
    - Hodgkin's lymphoma
    - Postoperative
  - B. *Extrahepatic*
    - Bile duct stone, stricture
    - Parasite (round worm)
    - Trauma to bile duct
    - Bile duct obstruction due to tumour (bile duct, pancreas, duodenum)
    - Secondaries in liver or at porta-hepatis
    - Pancreatitis
    - Choledochal cyst

- Anaemia with mild jaundice
- Freshly voided urine is not yellow, becomes yellow on standing due to conversion of excessive urobilinogen in the urine to urobilin on oxidation
- Preceding history of fever (malaria, viral), or intake of drugs if patient is G6PD deficient or intake of heavy metals.
- Typical facies, e.g. chipmunk facies seen in

thalassaemia due to excessive marrow expansion leading to frontal bossing and maxillary marrow hyperplasia

- Mild hepatosplenomegaly. The liver is nontender
- No pruritus or itching. No xanthelasma/xanthomatosis
- Peripheral blood film examination and other tests for haemolysis will confirm the diagnosis.

**128. What is differential diagnosis of hepatocellular jaundice?**

**Ans.** Common causes of hepatocellular jaundice are differentiated in Table 1.35.

**129. What are clinical characteristic of obstructive jaundice?**

**Ans.** The clinical characteristics are;

- Deep yellow or greenish yellow jaundice – called *surgical jaundice*
- Pruritus or itching present due to retention of bile salts
- Urine is dark coloured due to excretion of bile pigments but stools are clay-coloured (acholic)
- There may be associated pain abdomen, severe, colicky with intermittent jaundice, if bile duct stone is the cause
- Gall bladder is palpable if bile duct is obstructed either by an impacted stone or by carcinoma of head of pancreas
- Slowing of pulse rate or bradycardia may occur due to retention of bile salts
- Fever, shaking chills and rigors with jaundice indicate cholangitis
- In long-standing obstructive jaundice, xanthomas, weight loss, malabsorption or steatorrhoea may occur
- Conjugated hyperbilirubinaemia with dilatation of intrahepatic or extrahepatic ducts on USG confirm the diagnosis.

**130. What are characteristics of various viral hepatitis?**

**Ans.** The characteristics of viral hepatitis are enlisted in Table 1.36.

**131. What are causes of acute hepatitis?**

**Ans.** Hepatitis occurs due to a variety of infective and noninfective causes (Table 1.37).

**132. What are causes of prolonged jaundice (i.e. duration > 6 months)?**

**Ans.** Causes of prolonged jaundice are as follows:

**Table 1.35:** Differential diagnosis of hepatocellular jaundice

<i>Viral hepatitis</i>	<i>Autoimmune hepatitis</i>	<i>Alcoholic hepatitis</i>	<i>Carcinoma of liver</i>	<i>Drug induced</i>
<ul style="list-style-type: none"> <li>• Fever followed by jaundice. As the jaundice appears, fever disappears</li> <li>• Anorexia, nausea and vomiting, distaste to food and smoking</li> <li>• Arthralgia, myalgia, headache, pharyngitis, cough, fatigue, malaise</li> <li>• Dark coloured urine and clay-coloured or normal coloured stool</li> <li>• History of exposure to a patient with jaundice or use of contaminated food or I.V. injection/ blood transfusion or sexual contact, etc.</li> <li>• <i>Hepatomegaly</i>. Liver is moderately enlarged, soft, tender, smooth</li> <li>• Splenomegaly in 20% cases only</li> </ul>	<ul style="list-style-type: none"> <li>• Insidious onset. Chronic course</li> <li>• Common in females</li> <li>• Fever with jaundice, anorexia, fatigue, arthralgia, vitiligo, epistaxis. Amenorrhoea is the rule</li> <li>• Sometimes a “<i>cushingoid</i>” face with acne, hirsutism, pink cutaneous striae</li> <li>• Bruises may be seen</li> <li>• Hepatosplenomegaly, spider telangiectasis are characteristic</li> <li>• Other autoimmune disorders maybe associated</li> <li>• Serological tests for specific auto-antibodies confirm the diagnosis</li> </ul>	<ul style="list-style-type: none"> <li>• History of alcoholism</li> <li>• Anorexia, weight loss</li> <li>• Stigmata of chronic liver disease (spider naevi, palmar erythema, gynecomastia, testicular atrophy, Dupuytren’s contractures, parotid enlargement) may be present</li> <li>• Jaundice with enlarged tender liver</li> <li>• May be associated with other manifestations of alcoholism, e.g. cardiomyopathy, peripheral neuropathy</li> </ul>	<ul style="list-style-type: none"> <li>• Common in old age</li> <li>• Progressive jaundice with loss of appetite and weight</li> <li>• Liver enlarged, tender, hard, nodular. Hepatic rub may be heard</li> <li>• Anaemia, fever lymphadenopathy in neck and marked cachexia present</li> <li>• Jaundice is deep yellow or greenish</li> <li>• Ascites may be present</li> <li>• Evidence of metastatic spread to lungs, bone, etc</li> <li>• USG and liver biopsy will confirm the diagnosis</li> </ul>	<ul style="list-style-type: none"> <li>• History of intake of hepatotoxic drugs, e.g. INH, rifampicin oral contraceptives</li> <li>• Malaise before the onset of jaundice</li> <li>• Occasionally rash, fever, arthralgia present</li> <li>• Liver is enlarged and tender</li> <li>• Tests for viral hepatitis are negative</li> </ul>

- Chronic hepatitis or cholestatic viral hepatitis, chronic autoimmune hepatitis
- Cirrhosis of liver
- Malignancy liver
- Haemolytic jaundice (e.g. thalassaemia)
- Congenital hyperbilirubinaemia
- Drug- induced
- Alcoholic hepatitis
- Primary biliary cirrhosis
- Wilson’s disease
- Obstructive jaundice (extrahepatic biliary obstruction).

### 133. What are complications of acute viral hepatitis?

**Ans.** Complications are common in type B or type C viral hepatitis; type A hepatitis usually resolves spontaneously. The complications are;

- Fulminant hepatitis – a dreadful complication
- Cholestatic viral hepatitis
- Relapsing hepatitis (transient subclinical infection)

- Chronic carrier state
- Chronic hepatitis
- Post-hepatitis syndrome (symptoms persist but biochemical investigations normal)
- Cirrhosis of the liver
- Hepatocellular carcinoma.

### 134. What is carrier state in hepatitis?

**Ans.** Some asymptomatic patients carrying the HbsAg for more than 6 months after the episode of acute hepatitis B are called *chronic carriers*. Carrier stage does not exist in hepatitis A and E. These carriers are potential source of transmission of infection.

### 135. How will you investigate a case with acute viral hepatitis?

**Ans.** Following are the investigations:

1. **TLC and DLC** may show leucopenia or lymphopenia, atypical lymphocytes may be seen. The ESR may be high.



**Table 1.36:** Distinguishing features of main hepatitis viruses

Virus	A	B	C	D	E
Group	Enterovirus	Hepadna	Flavivirus	Delta particle (incomplete virus)	—
Nucleic acid	RNA	DNA	RNA	RNA	RNA
Size	27 nm	40-42 nm	30-35 nm	35 nm	27 nm
Incubation period in weeks	2-6	4-26	2-20	5-9	3-8
<b>Spread</b>					
Faeco-oral	Yes	No	No	No	Yes
Parenteral (blood)	Uncommon	Yes	Yes	Yes	Yes
Saliva (kissing)	Yes	Yes	Yes	—	—
Sexual act	Uncommon	Yes	Uncommon	Yes	Unknown
Vertical transmission	No	Yes	Uncommon	Yes	No
<b>Chronic infection</b>					
Incidence	Not known	5-10%	>50%	—	—
Severity	Mild	Often severe	Moderate	Unknown	Mild to moderate
<b>Prevention</b>					
Active	Vaccine	Vaccine	No	Prevented by hepatitis B Virus infection	No
Passive	Immune serum globulins	Hyperimmune serum globulins	No		No
Prognosis	Good	Worst with age and debility	Moderate	Same as with hepatitis B	Good

**Table 1.37:** Causes of acute hepatitis

<b>Infective</b>	
• Viral, e.g. hepatitis A,B,C,D,E, Epstein-Barr virus, cytomegalovirus, herpes simplex and yellow fever virus	
• Postviral	
Reye's syndrome in children (aspirin-induced)	
• Nonviral, e.g. leptospira, toxoplasma, coxiella	
<b>Noninfective</b>	
• Drugs, e.g. paracetamol, halothane, INH, rifampicin, chlorpromazine, methyl dopa, oral contraceptives	
• Poisons, e.g. carbon tetrachloride, mushrooms, aflatoxin	
• Metabolic, e.g. Wilson's disease, pregnancy	
• Vascular, e.g. CHF, Budd-Chiari syndrome, oral contraceptives	

## 2. Hepatic profile

- Serum bilirubin raised, equally divided between conjugated and unconjugated fractions, or sometimes conjugated fraction may predominate (cholestatic phase).

- Serum transaminases (SGOT/SGPT) are raised more than ten times (400-4000 IU).
- Serum alkaline phosphatase may or may not be raised; if raised, indicates cholestasis
- Plasma albumin is normal, may become low if jaundice is prolonged.
- Prothrombin time is normal, if increased, indicates extensive hepatocellular damage and bad prognosis
- Urine may show;
  - Urobilinogen in urine, appears during preicteric phase, disappears with onset of jaundice and reappears during recovery.
  - Bilirubinuria occurs during subclinical stage
  - Presence of bile salt and bile pigment indicates cholestasis
  - Stool may be normal coloured or clay-coloured (obstructive jaundice)

**Table 1.38:** Serological tests

Stage		HbsAg Anti-HBc		
		IgM	IgG	Anti HBs
Incubation period	(+)	(+)	(-)	(-)
Acute hepatitis	(+)	(+)	(-)	(-)
early				
Established	(+)	(+)	(+)	(-)
Convalescence				
3-6 weeks	(±)	(±)	(+)	(±)
6-9 months	(-)	(-)	(+)	(+)
Past-infection more than 1 year	(-)	(-)	(+)	(+)
Chronic infection				
Usual	(+)	(-)	(+)	(-)
Immunisation without infection	(-)	(-)	(-)	(+)

(+) positive; (-) negative; (±) positive or negative  
 Note: Presence of HbeAg indicate active replication of virus at the onset, it followed by production of anti-Hbc. Persistence of HbeAg indicates infectivity

- Ultrasound of liver** may reveal hepatomegaly with normal echotexture. CT scan is not superior to USG.
- Serological tests** (Table 1.38) These are done in hepatitis B.

### 136. What are extrahepatic manifestations of hepatitis B virus infection?

**Ans.** Extrahepatic manifestations are as follows:

- Serum sickness like syndrome
- Polyarthrititis
- Acute glomerulonephritis (immune complex)
- Atypical pneumonia
- Aplastic anaemia or agranulocytosis
- Autoimmune haemolytic anaemia
- Guillain-Barre syndrome
- Skin rashes (urticaria).

### 137. What is acute fulminant hepatitis? How does it present clinically?

**Ans.** Acute fulminant hepatitis is said to be present when a previously healthy person develops acute hepatitis and goes into acute hepatic insufficiency/failure within 2 weeks of illness. This is due to acute massive necrosis (acute yellow atrophy) with shrinkage of liver (liver span <10 cm on USG).

The causes are; Type B, C and D viral infection, drugs, pregnancy, Wilson's disease and liver poisons (mushrooms, carbon tetrachloride, phosphorous) and Reye's syndrome in children.

The symptoms and signs of acute fulminant hepatitis are due to acute hepatic encephalopathy without stigmata of the liver disease and signs of portal hypertension.

### 138. What is chronic hepatitis? What are its causes?

**Ans.** It is defined as an inflammation of the liver (acute viral hepatitis) lasting for  $\geq 6$  months. The causes are;

- Autoimmune hepatitis
- Hepatitis B, C, D
- Drug-induced hepatitis
- Wilson's disease
- Alcoholic hepatitis
- Alpha-1 antitrypsin deficiency

The diagnosis of chronic hepatitis is made when clinical and biochemical evidence of hepatitis (e.g. jaundice, raised liver enzymes) persist for >6 months. The diagnosis is confirmed by liver biopsy and blood serology.

### 139. Whom will you advise prophylaxis against hepatitis B (Table 1.39)

**Ans.** The indications are given in Table 1.39. Recently there has been mass prophylaxis program for hepatitis B in general population in India.

**Table 1.39:** Indications for hepatitis B vaccination in endemic areas

- **Parenteral drug abusers**
- **Male homosexuals**
- **Close contacts** (relatives or sexual partners) of infected persons
- **Patients receiving maintenance dialysis**
- **Laboratory staff**
- **Medical personnel**
  - Dentists
  - Surgeons/obstetricians
- **Medical /paramedical staff of:**
  - Intensive care department
  - Accident and emergency department
  - Endoscopy units
  - Oncology units
- **Nursing staff** involved in care of such patients

## CASE 13: ASCITES

### History

The patient (Fig. 1.13) presented with progressive distension of abdomen with abdominal discomfort and dyspnoea. No history of jaundice or haematemesis. No history of oedema feet or puffiness of face. No history of palpitation, PND or orthopnoea. No past history of jaundice or rheumatic fever. No history of pain chest, cough with expectoration or haemoptysis.

### Points to be Noted on History

- Onset and progression of symptoms
- Past history of jaundice, haematemesis, RHD, tuberculosis, etc.
- Personal history-alcoholism
- Family history, e.g. cirrhosis, Wilson's disease, haemachromatosis.

### General Physical Examination

Look for the followings;

- Face: vacant look, emaciated face and sunken cheeks indicate cirrhosis of the liver
- Mental features, e.g. confusion, disorientation, disturbed sleep pattern, bizarre handwriting, disturbed speech with jaundice indicate hepatic encephalopathy
- Puffiness of face with periorbital oedema. It occurs in nephrotic syndrome
- Generalised or localised lymph adenopathy (e.g. tubercular, malignancy collagen vascular disorders)
- Raised JVP and cyanosis (congestive heart failure, constrictive pericarditis)
- Cyanosis, clubbing of fingers (e.g. bacterial endocarditis, hepatic encephalopathy)
- Stigmata of chronic liver disease, e.g. muscle wasting, gynaecomastia, testicular atrophy, loss of axillary and pubic hair, parotid enlargement and Dupuytren's contractures)
- Palmar erythema or painful fingertips or gangrene or flapping tremors
- Pedal oedema
- Signs of multiple nutrients deficiency e.g. angular stomatitis, cheilosis, anaemia, atrophic or bald tongue, muscle flabbiness, wasting and pigmentation of tongue and mucous membranes.



**Fig. 1.13:** A patient with ascites. Note the distended abdomen with everted umbilicus and a ventral hernia (↓) above the small umbilical hernia

### Clinical Presentations

- Often considerable number of patients with ascites may go unnoticed for weeks or months either because of coexistent obesity or because the ascites formation has been insidious, without pain or localising symptoms.
- Ascites may first be noticed by the patient as an abdominal swelling with progressive increase in belt or size of clothing.
- Progressive abdominal distension due to ascites produces sensation of stretching or pulling of the flanks or groins and vague low back pain.
- Tense ascites may produce an increase in intra-abdominal pressure resulting in indigestion and heart burn due to gastroesophageal reflux; or dyspnoea, orthopnoea and tachypnoea due to elevated domes of diaphragm and abdominal wall hernias (inguinal or abdominal).
- Patient may complain of respiratory embarrassment due to massive ascites or right sided pleural effusion due to leakage of ascitic fluid through lymphatic channels in diaphragm. A large pleural effusion obscuring the most of the lung may occasionally develop, is known as *hepatic hydrothorax*.

### Systemic Examination

#### Inspection

- Fullness of flanks or tense abdominal distension
- The umbilicus is either transversely slit e.g. smiling umbilicus (moderate ascites) or everted with or without umbilical hernia (massive ascites)
- Prominent distended veins over the abdomen or around umbilicus (caput medusae) in a patient with cirrhotic portal hypertension or inferior vena cava obstruction
- Ventral, umbilical or inguinal hernia may or may not be seen
- There may be a mark of tapping of ascites (a mark with staining of tincture)

#### Palpation

- Increased abdominal girth
- Tenderness of abdomen in peritonitis with ascites
- Flow of blood in distended veins is away from the umbilicus in portal hypertension and from below upwards in IVC obstruction
- Palpable spleen in a patient with ascites (by dipping method) indicate portal hypertension
- Hepatomagaly. It indicates Budd-Chiari syndrome (malignancy or past necrotic nodular conolasis)

#### Percussion

- Percussion note is dull. Dullness is more marked in flanks with central sparing
- *Shifting dullness* is present in moderate ascites but becomes absent in huge ascites
- Fluid thrill is present in huge ascites, moderate ascites and localised ascites but absent in mild ascites
- Puddle's sign (dullness around umbilicus in knee-elbow position) is positive in mild ascites

#### Auscultation

- A venous hum around umbilicus indicate cirrhotic portal hypertension (Cruveilhier-Bombgarten's syndrome)
- A bruit over the liver indicate malignancy or recent biopsy has been taken.

**140. How do you define ascites?**

**Ans.** Normal amount of fluid in the peritoneal cavity is 100-150 ml of lymph, not detected by any means. Abnormal collection of fluid (>300 ml) in the peritoneum is called *ascites*. This amount is detected on USG abdomen. Significant amount of fluid (>500 ml) produces fullness of flanks on lying down position, is detected clinically. Larger amount of fluid (e.g. 1 litre) produces horse-shoe shape of the abdomen. Tense ascites means the peritoneal cavity is filled with free fluid producing cardio-respiratory embarrassment.

**141. What are causes of ascites?**

**Ans.** Ascites occurs due to transudation of fluid into peritoneum in hypoproteinaemic states or exudation into peritoneum by inflammation or infiltration of peritoneum by malignant process. The common causes are given in Tables 1.40 and 1.41.

**Table 1.40:** Causes of ascites

Systemic (ascites with oedema)	Local (ascites only without oedema)
<ul style="list-style-type: none"> <li>• Nephrotic syndrome</li> <li>• Cirrhosis of the liver</li> <li>• Hypoproteinaemia: nutritional or following chronic diarrhoea or mal-absorption</li> <li>• Congestive heart failure or constrictive pericarditis</li> <li>• Malignancy liver</li> <li>• Meig's syndrome (ovarian tumour)</li> <li>• Hypothyroidism</li> </ul>	<ul style="list-style-type: none"> <li>• Peritonitis (serous, exudative)</li> <li>• Tuberculosis</li> <li>• Malignancy with secondaries in peritoneum</li> <li>• Spontaneous bacterial peritonitis</li> <li>• Pancreatitis</li> <li>• Portal vein thrombosis</li> <li>• Hepatic vein thrombosis (Budd-Chiari syndrome)</li> <li>• Chylous ascites</li> </ul>

**142. What is differential diagnosis of ascites?**

**Ans.** The differential diagnosis of ascites depends on the cause of ascites and whether ascites is a part of generalised *anasarca* (ascites, oedema, fluid in serous cavities) or is localised.

1. **Ascites of nephrotic syndrome:** Puffiness of face in the morning, pitting ankle oedema, slowly developing ascites with or without anaemia indicate ascites to be of renal origin. The massive albuminuria confirms the diagnosis.

**Table 1.41:** Causes of ascites depending on the nature of fluid**Transudate (serum/ascitic fluid albumin gradient > 1.1)**

- Non-inflammatory fluid, serous or straw coloured
- Fluid protein content <3.0 g/dl (or <50% of serum proteins)
- Specific gravity low or normal
- Occasional cell, mostly mesothelial
- Serum-ascites albumin gradient >1.1 g/dl (serum albumin minus ascitic fluid albumin)

**Causes**

- Nephrotic syndrome
- Congestive heart failure, pericardial effusion
- Hypoproteinaemia, protein-losing states
- Cirrhosis of the liver
- Meig's syndrome

**Exudate (serum/ascitic fluid albumin gradient > 1.1)**

- Inflammatory thick, turbid or mucinous, haemorrhagic or straw coloured fluid
- Protein content >3.0 g/dl (>50% of serum proteins)
- Specific gravity is high
- Cell count (100-1000 cells/mm<sup>3</sup>), mostly either mononuclear or neutrophils
- Serum-ascites albumin gradient <1.1 g/dl

**Causes**

- Peritonitis, e.g. pyogenic, tubercular, malignant, subacute bacterial
- Leukaemias, lymphomas
- Chylous ascites
- Budd-Chiari syndrome
- Pancreatitis (pancreatic ascites)

2. **Ascites due to cirrhosis of the liver:** Past history of jaundice or chronic liver disease, with history of recent episode of haematemesis and jaundice in a patient with ascites suggest cirrhosis. The gynaecomastia, loss of axillary and pubic hair, weakness, weight loss are stigmata of chronic liver disease. Prominent abdominal veins, splenomegaly suggest portal hypertension due to cirrhosis.
3. **Ascites due to hypoproteinaemia:** Anaemia, multiple deficiencies, muscle flabbiness and atony of muscles with ascites and oedema indicate hypoproteinaemia to be its cause. The patient may have history of chronic diarrhoea or recurrent diarrhoea.
4. **Ascites of congestive heart failure:** Raised JVP, tender hepatomegaly, dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea (PND),



cardiomegaly with or without murmurs, ascites, oedema with or without peripheral cyanosis are points in favour of congestive heart failure as the cause of ascites.

5. **Tubercular ascites:** A slow developing ascites with anorexia, low grade fever, common occurrence in females than males, night sweats and evening rise of fever with or without any evidence of tuberculosis elsewhere are points in favour of tubercular ascites if it develops in young age.
6. **Malignant ascites:** Rapid filling tense ascites in old age with decrease or loss of appetite, marked cachexia, haemorrhagic nature of ascites could be due to malignancy anywhere in the abdomen with secondaries in the peritoneum.

#### 143. What is chylous ascites? What are its causes?

**Ans.** It is the presence of milky fluid containing lymph in the peritoneal cavity. Milky fluid (turbidity) may be due to large number of cells (e.g. leucocytes, degenerated cells or tumour cells) or due to increased amount of protein content called *pseudochylous*.

##### Causes

Chylous ascites is most commonly due to obstruction to the lymphatics or thoracic duct, contains a large amount of triglycerides, and results from;

1. Trauma or penetrating abdominal injury to the thoracic duct
2. Tumours
3. Tuberculosis with lymphadenitis
4. Filariasis (filarial worms obstructing the lymphatics).

Turbidity of fluid disappears after extraction with ether; a diagnostic clue to the presence of fat and differentiates it from pseudochylous ascites.

*Pseudochylous ascites* refers to increased amount of proteins and calcium in the fluid leading to turbidity which is not dissolved by ether.

*Chyliform ascites* means a large number of cells (leucocytes, degenerated epithelial cells or tumour cells) as the cause of turbidity which disappears on extraction with alkali.

#### 144. What is mucinous ascites?

**Ans.** Rarely, ascitic fluid may be mucinous (gelatinous)

in character, giving lobulated (jelly like mass) appearance to the ascites. The fluid thrill and shifting dullness are absent. It is difficult to aspirate (ascitic tap is dry). It may be either due to *pseudomyxoma peritonei* (rupture of mucocoele of appendix or mucinous ovarian cyst) or rarely colloid carcinoma of stomach or colon with peritoneal metastases.

#### 145. What important points will you ask in history from a patient with ascites?

**Ans.** The followings points are to be noted in a case of ascites:

- Onset, e.g. sudden or gradual
- Past history of rheumatic fever, joint pain, jaundice, alcoholism, haematemesis or melena. Low grade fever or past history of tuberculosis or polyarthritis
- Decrease or loss of appetite
- Diet and nutrition
- Cough and hemoptysis (present or past)
- Loss of weight
- Prolonged history of diarrhoea >3 months, alteration in bowel habits
- Pain abdomen (acute pancreatitis)
- History of puffiness of face or oedema.

#### 146. What is refractory ascites?

**Ans.** It is defined as ascites nonresponsive to optimal medical therapy; occurs in 10-20% cases. The factors that lead to refractory ascites are;

- i. Noncompliance of salt restriction
- ii. Hepatorenal syndrome, e.g. functional renal failure in cirrhosis of the liver
- iii. Low serum sodium or failure of diuretic therapy
- iv. Infections or subacute bacterial peritonitis
- v. Superimposition of hepatoma
- vi. GI bleeding
- vii. Development of hepatic or portal vein thrombosis.

#### 147. What are physical signs of ascites?

**Ans.** Read "Clinical Methods in Medicine" by Dr SN Chugh.

#### 148. What are physical signs of mild, moderate and massive ascites?

**Ans.** The signs are given in the Table 1.42



**Table 1.42:** Physical signs in various grades of ascites

Grade	Signs
0 Minimol	Puddle's sign
1 Mild	Shifting dullness present fluid thrill absent
2 Moderate	Shifting dullness and fluid thrill present
3 Massive	Fluid thrill present, shifting dullness absent

N.B. Localised ascites will behave like massive ascites, hence, in this also fluid thrill will be present and shifting dullness absent.

#### 149. What are the causes of rapid filling of ascites?

**Ans.**

- Malignancy (primary and secondary)
- Tuberculosis
- Chylous
- Spontaneous bacterial peritonitis
- Budd-Chiari syndrome.

#### 150. What are causes of purulent and hemorrhagic ascites?

**Ans.** They are depicted in Table 1.43.

**Table 1.43:** Purulent vs haemorrhagic ascites

Purulent ascites	Haemorrhagic ascites
<ul style="list-style-type: none"> <li>• Pyogenic peritonitis</li> <li>• Septicaemia</li> <li>• Ruptured amoebic liver abscess</li> <li>• Pelvic inflammatory disease</li> <li>• Penetrating abdominal trauma with introduction of infection</li> </ul>	<ul style="list-style-type: none"> <li>• Abdominal trauma or trauma during tapping of ascites</li> <li>• Malignancy of peritoneum (primary or secondary)</li> <li>• Tubercular peritonitis</li> <li>• Bleeding diathesis</li> <li>• Acute haemorrhagic pancreatitis</li> </ul>

#### 151. What are the causes of ascites disproportionate to oedema feet (ascite precox)?

**Ans.** These are as follows:

- Constrictive pericarditis
- Restrictive cardiomyopathy
- Hepatic vein thrombosis
- Cirrhosis of liver
- Tubercular peritonitis
- Intra-abdominal malignancy
- Meig's syndrome

#### 152. What are the causes of hepatosplenomegaly with ascites?

**Ans.** Hepatosplenomegaly with ascites indicates lymphoreticular malignancy, leukaemia, malignancy of liver, secondaries in the liver, hepatic vein thrombosis (Budd-Chiari syndrome), postnecrotic cirrhosis, congestive heart failure, pericardial effusion.

#### 153. How will you investigate a patient with ascites?

**Ans.** Investigations are done to confirm the diagnosis and to find out its cause. These include;

1. *Blood examination:* Anaemia may be present. Presence of neutrophilic leucocytosis indicates infection.
2. *Urine examination:* Massive albuminuria (>3.5 g/day) is present in nephrotic syndrome. Small amount of proteinuria occurs in pericardial effusion and congestive heart failure.
3. *Stool for occult blood:* If present, may indicate gastrointestinal malignancy as the cause of ascites.
4. *Ultrasonography:* It is of proven value in detecting ascites, presence of a masses, evaluation of size of liver and spleen, portal vein diameter and presence of collaterals.
5. *Plain X-ray abdomen* in standing position is useful. It may show ground glass opacity or diffuse haziness with loss of psoas muscle shadow. It may show intestinal obstruction (3-5 fluid levels in step-ladder pattern), raised right dome suggests either amoebic liver abscess or hepatoma.
6. *Diagnostic paracentesis:* 50-100 ml of ascitic fluid is withdrawn with the help of a needle and biochemically analysed to establish the aetiology of ascites and to plan its treatment. It is also sent for bacteriological examination. The differences between transudative and exudative ascites with their respective causes have already been discussed.
7. *Serum-ascites albumin gradient:* The albumin in serum and ascitic fluid is determined to calculate the gradient. The serum albumin *minus* ascitic fluid albumin determines the gradient. The gradient >1.1 g/dl indicates transudative ascites and <1.1 g/dl indicates exudative ascites. The fluid protein <50% of serum protein also indicates transudate; while  $\geq 50\%$  indicates exudate.

8. Further investigations are done to find out the cause, e.g. serum proteins, serum cholesterol for nephrotic syndrome, X-ray chest, ECG, Echo for congestive heart failure/pericardial effusion, liver function tests and tests for portal hypertension.

**154. What does paracentesis mean? What are its indications?**

**Ans.** Paracentesis means removal of fluid. Paracentesis of ascitic fluid is indicated as follows:

- i. *Diagnostic*: A diagnostic tap of ascitic fluid is done by putting the needle in the flank in one of lateral positions. The fluid removed is 50-100 ml for diagnostic purpose, i.e. for biochemical, cytological and bacteriological analysis.
- ii. *Therapeutic*: It is done as a part of treatment. Ascitic fluid is rich in proteins, hence should not be routinely tapped. It is removed if patient has cardiorespiratory embarrassment (acute respiratory distress with tachycardia). The amount of fluid removed depends on the relief of symptoms or maximum of 3-5 litres of fluid may be removed in one setting. Repeated tapping should be avoided unless absolutely necessary as this may predispose to secondary infection of peritoneum and also causes protein loss.
- iii. *Refractory ascites* (nonresponse to treatment)
- iv. Paracentesis is attempted before needle biopsy of liver, ultrasonography or for better palpation of underlying viscera.

**155. What are complications of paracentesis?**

**Ans.** Common complications of paracentesis are as follows:

- Sudden withdrawal of a large amount of fluid may lead to dilatation of splanchnic blood vessels with subsequent development of shock.
- Introduction of infection (peritonitis) if sterile precautions are not observed.
- Hypoproteinaemia. Ascitic fluid is rich in proteins, repeated large amount of aspiration may lead to development of hypoproteinaemia.
- *Precipitation of hepatic coma*. Sudden withdrawal of ascites in a patient with cirrhotic portal hypertension may precipitate hepatic encephalopathy
- *Constant oozing of the ascites* due to formation of a track (especially in tense ascites).

**156. What are sequelae/complications of a ascites?**

**Ans.** These are as follows:

- Right sided pleural effusion due to leakage of ascitic fluid through lymphatic channels in the diaphragm.
- Spontaneous bacterial peritonitis
- Abdominal hernia (umbilical, inguinal) and diverticulation of recti due to tense ascites as a result of increased intraabdominal pressure
- Functional renal failure
- Mesenteric venous thrombosis.

**Note:** for differentiation of ascites from ovarian cyst and distended urinary bladder, read clinical methods in Medicine by Prof. S.N. Chugh.

**CASE 14: HEPATOMEGALY**

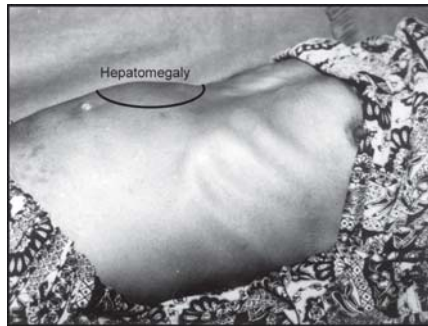
The patient (Fig. 1.14) presented with pain in the abdomen especially in right hypochondrium with swinging temperature, chills and rigors of 2 weeks duration. There was past history of loose motions and blood. Pain was more marked in left lateral position.

**Points to be noted in History**

- Present history of dysentery or GI disorder
- Any history of bleeding from any site
- History of fever, pigmentation, neck swelling, jaundice
- Full drug history
- Past history of tuberculosis, jaundice, diabetes, RHD
- Personal history, e.g. alcoholism
- Nutritional history
- Family history of polycystic disease.

**General Physical Examination**

- Assess the nutritional status
- Examine neck for lymph nodes, JVP
- Look at the skin for purpuric spots, ecchymosis, bruises, pigmentation
- Note anaemia, cyanosis, jaundice, palmer erythema, spider angiomas
- Look for stigmata of chronic liver disease
- Note pedal oedema
- Examine vitals, e.g. respiration, pulse, temperature and BP



**Fig. 1.14:** A patient with hepatomegaly

**Clinical Presentations**

Patients having hepatomegaly present with;

1. No symptoms (asymptomatic) Hepatomegaly is detected during routine examination.
2. Pain in right upper quadrant: It occurs in acute hepatomegaly due to stretching of the capsule of the liver which is pain-sensitive structure.
3. Mass in right hypochondrium.
4. Patients may present with fever, jaundice, distaste for food, dark urine and sometimes pruritus.
5. Patient may present, acute pain with fever and chills. This may occur following an episode of dysentery.

**Systemic Examination***Inspection*

- A right upper quadrant fullness due to mass that moves with respiration (present in this case)
- Umbilicus is normal unless ascites present
- Normal abdominal movements
- Hernia sites are usually normal
- Prominent abdominal veins and collateral with flow away from umbilicus suggest portal hypertension

*Palpation*

- Define the mass and study its characteristics, e.g. solid or cystic, smooth or irregular, soft, firm or hard, tender or nontender, etc. Note whether it is pulsatile or not
- Elicit intercostal tenderness (thumping sign). It was positive in this case.
- Elicit the signs of ascites if suspected
- Palpate the abdomen for other mass or masses such as spleen or lymph nodes.

*Percussion*

- Define upper and lower borders of the liver and calculate the liver span was 22 cm in this case
- Hydatid sign if hydatid cyst is suspected
- Percuss flanks for ascites.

*Auscultation*

- A bruit indicates a vascular hepatic tumour
- A rub indicates hepatic infarction or a nodular liver
- A venous hum around umbilicus indicates portal hypertension
- Auscultate for bowel sounds.

**157. What is your clinical diagnosis and why?**

**Ans.** In view of painful mass in right hypochondrium with swinging temperature and chills, positive intercostal tenderness with massive hepatomegaly without Jaundice and signs of portal hypertension; and past history of dysentery the diagnosis of amoebic liver abscess is most likely.

**158. How do you define hepatomegaly?**

**Ans.** Liver is placed just below the right dome of

diaphragm and its edge is normally palpable on deep inspiration in right hypochondrium in some people and in children. The palpable liver does not mean hepatomegaly because if liver is displaced downwards due to any cause (emphysema, subphrenic abscess) it becomes palpable. Therefore, before commenting on hepatomegaly, the upper border must be defined by percussion in midclavicular line. Upper border of liver dullness is in 5th intercostal space.

Hepatomegaly refers to actual enlargement of liver (enlarged liver span) without being displaced downwards, i.e. the upper border of liver dullness stays as normal.

**159. What are the causes of palpable liver without its actual enlargement?**

**Ans.** This denotes downwards displacement of normal liver due to;

- Emphysema
- Thin and lean person
- Subphrenic abscess (right side)
- Visceroptosis
- Any mass or fluid interposed between liver and the diaphragm will push liver downwards e.g. subpulmonic effusion. Massive right sided pleural effusion or pneumothorax.

**160. Where are the points to be noted in hepatic enlargement?**

**Ans.** Following are important points:

1. *Extent of enlargement.* Liver span should be defined. Normal liver span is 10-14 cm. Less than 10 cm is considered as acute fulminant hepatitis (acute yellow atrophy) and >14 cm is taken as hepatomegaly.
2. *Movements with respiration.* Liver always moves with respiration, i.e. descends 1-3 cm downwards with deep inspiration.
3. *Tenderness* (tender or nontender). Tender hepatomegaly suggests acute enlargement or infarction.
4. *Edge* (sharp or blunt)
5. *Surface* (smooth, irregular or nodular)
6. *Consistency* (soft, firm, hard)
7. *Upper border of liver dullness* (normal or shifted)
8. *Whether left lobe* is enlarged or not. Is there any enlargement of caudate lobe?
9. Any *rub, bruit, venous hum*.
10. Any *pulsation* (intrinsic or transmitted).

**161. What are the causes of hepatomegaly?**

**Ans.** Table 1.44 explains the causes of hepatic enlargement.

**162. What are the common causes of mild to moderate hepatomegaly?**

**Ans.** They are;

- Typhoid fever, tuberculosis

**Table 1.44:** Aetiology of hepatic enlargement

**1. Vascular**

- Congestive heart failure (CHF)
- Pericardial effusion or constrictive pericarditis
- Hepatic vein thrombosis (Budd-Chiari syndrome)
- Haemolytic anaemia

**2. Bile duct obstruction (Cholestasis)**

- Bile duct stone
- Tumour

**3. Infiltrative**

- Leukaemias (acute and chronic leukaemia especially chronic myeloid leukaemia)
- Lymphoma
- Fatty liver (e.g. alcoholism, diabetes, malnutrition)
- Amyloidosis
- Fat storage diseases such as Gaucher's disease, Niemann-Pick's disease in children.
- Granulomatous hepatitis (e.g. typhoid, tuberculosis and sarcoidosis)

**4. Parasitic**

- Malaria
- Kala azar
- Hydatid disease
- Amoebic liver abscess

**5. Infective/inflammatory**

- Hepatitis
- Typhoid fever

**6. Tumours**

- Hepatocellular carcinoma
- Secondaries or metastatic deposits in liver

**7. Rare**

- Polycystic disease of the liver
- Haemangioma of liver
- A large hepatic cyst

- Leukaemias
- Congestive splenomegaly (e.g. CHF, pericardial effusion)
- Budd-Chiari syndrome
- Haemolytic anaemia
- A haemangioma or congenital cyst
- Fatty liver
- Postnecrotic cirrhosis

**163. What is differential diagnosis?**

**Ans.** The followings are differential conditions:

*Congestive Hepatomegaly*

It is due to chronic venous congestion of the liver as a result of congestive heart failure due to any cause, (i.e. constrictive pericarditis, pericardial effusion) and hepatic



vein thrombosis (Budd-Chiari syndrome). Symptoms of dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea and cough with physical signs such as raised JVP, cyanosis, peripheral oedema, crackles at both lung bases, heart murmurs, cardiomegaly and hepatomegaly indicate congestive heart failure. Nonvisible apex, pulsus paradoxus, low pulse pressure, widening of cardiac dullness and dullness of 2nd and 3rd left space, feeble heart sounds with other peripheral signs of congestive heart failure indicates hepatomegaly due to either constrictive pericarditis or pericardial effusion. In hepatic vein thrombosis (Budd-Chiari syndrome), there is an intractable ascites, jaundice, prominent abdominal veins and collaterals formation due to development of portal hypertension. Hepatomegaly is a part of the syndrome.

In these congestive states, liver is moderately or massively enlarged, tender, has smooth surface and round well defined edge. Further investigations should be done to confirm the diagnosis. Management depends on the underlying cause.

#### *Inflammatory Hepatomegaly*

Inflammation of liver due to hepatitis or typhoid fever produces enlargement of liver. In hepatitis, there is history of fever, distaste for food, nausea, vomiting followed by jaundice and pain in right hypochondrium. Typhoid fever is characterised by moderate to high grade fever, abdominal symptoms (nausea, vomiting, diarrhoea with or without blood), tenderness of abdomen, rose spots and slow pulse rate. At about 7 to 10th day of illness, spleen also becomes enlarged.

Liver in inflammatory disorders shows mild to moderate enlargement, is tender and has smooth surface. Further investigations are required to confirm the respective inflammatory cause.

#### *Infiltrative Hepatomegaly*

Liver becomes enlarged when it gets infiltrated with leukaemic cells or lymphoma cells or with fat and glycogen. Fatty infiltration of liver occurs in pregnancy, malnutrition, diabetes mellitus and alcoholism. Fatty liver is mildly enlarged, non-tender and has smooth surface. In leukaemia, there is evidence of anaemia, bleeding tendency (purpuric spots, ecchymosis, epistaxis, bruising

etc), fever, lymph node enlargement and splenomegaly; while fever with hepatosplenomegaly and lymphadenopathy are characteristics of lymphoma. Peripheral blood film examination will confirm the diagnosis. In these disorders, liver is moderately enlarged, soft to firm in consistency, nontender with smooth surface. Further investigations are needed to confirm the diagnosis.

#### *Hepatomegaly Due to Parasitic Infection/Infestations*

Malaria, kala-azar, hydatid disease and amoebic infection can produce hepatomegaly by various mechanisms. Malaria produces massive enlargement of liver along with other characteristics, such as fever of several days duration with classical bouts on alternate days with shaking chills and rigors. Jaundice is also common due to hepatitis or haemolysis. There is splenomegaly. Hepatomegaly is non-tender. Peripheral blood film will confirm the diagnosis of this condition.

Fever, hyperpigmentation of skin, especially face and hands, hepatosplenomegaly and anaemia support the diagnosis of kala-azar in endemic area. The diagnosis can easily be confirmed by demonstrating the parasite in stained smears of aspirate of bone marrow, lymph nodes, spleen or liver or by culture of these aspirates.

Hydatid disease of liver produces cystic enlargement with positive hydatid sign on percussion with peripheral eosinophilia. USG is useful for confirming the diagnosis.

#### *Hematological Disorders*

All types of anaemia, especially haemolytic anaemia, lead to mild to moderate non-tender hepatomegaly. The presence of mild jaundice, dark coloured urine and stools with mild to moderate hepatosplenomegaly support the diagnosis of haemolytic anaemia. The diagnosis is further confirmed by tests for haemolysis and peripheral blood film examination. Malaria can also produce haemolysis, jaundice and hepatomegaly as already discussed.

#### *Tumours of Liver*

The tumours (primary or secondary) can enlarge the liver. Liver in malignancy is massively enlarged, tender and has nodular surface and hard consistency. Friction rub may be audible in some cases. Jaundice, pruritus may or may not be present, depending on the presence



or absence of cholestasis. USG and biopsy of liver will confirm the diagnosis.

#### *Hepatomegaly Due to Diseases of Liver*

Post-hepatic or post-necrotic cirrhosis can produce non-tender, mild to moderate hepatomegaly with other stigmata of cirrhosis and portal hypertension (muscle wasting, loss of axillary and pubic hair, gynaecomastia, palmar erythema, spider angiomas, ascites, caput medusae and splenomegaly). The diagnosis is confirmed by liver biopsy and by biochemical and radiological tests.

#### **164. What are the causes of tender hepatomegaly?**

**Ans.** Causes are as below:

- Acute viral hepatitis
- Amoebic liver abscess
- Congestive hepatomegaly (e.g. CHF, constrictive pericarditis, pericardial effusion, Budd-Chiari syndrome)
- Pyogenic liver abscess
- Malignancy of the liver
- Perihepatitis (e.g. after biopsy or hepatic infarct)
- Infected hydatid cyst.

#### **165. What are the causes of enlargement of left lobe?**

**Ans.** Causes are as below:

- Amoebic liver abscess (left lobe abscess)
- Hepatoma
- Metastases in liver.

#### **166. What are different consistencies of the liver?**

**Ans.** Table 1.45 explains the answer.

**Table 1.45:** Differential diagnosis of hepatomegaly depending on consistency of liver

Consistency	Causes
Soft	Congestive heart failure, viral hepatitis, fatty liver, acute malaria, viscerosplenic (drooping of liver)
Firm	Cirrhosis, chronic malaria and kala-azar, hepatic amoebiasis, lymphoma
Hard	Hepatocellular carcinoma, metastases in liver, chronic myeloid leukaemia, myelofibrosis

#### **167. What are the causes of irregular surface of liver?**

**Ans.** Followings are causes:

- Cirrhosis (micronodular or macronodular)
- Secondaries in the liver
- Hepatocellular carcinoma
- Hepatic abscesses (pyogenic, amoebic)
- Multiple hepatic cysts.

#### **168. What are the causes of massive hepatomegaly?**

**Ans.** Massive hepatomegaly means enlargement > 8 cm below the costal margin. The causes are:

1. Malignancy liver (primary or secondary)
2. Amoebic liver abscess
3. Chronic malaria and kala-azar
4. Hepatitis (sometimes)
5. Hodgkin's disease
6. Polycystic liver disease

N.B. Acute malaria does not hepatomegaly

#### **169. What are the causes of hepatic bruit and rub?**

**Ans.** Followings are the causes:

##### *Bruit*

- Hepatocellular carcinoma
- Haemangioma liver

##### *Rub*

- Following liver biopsy
- Hepatic infarction (embolic)
- Perihepatitis due to any cause
- Carcinoma of liver

#### **170. What do you understand by pulsatile liver? How will you demonstrate it?**

**Ans.** Pulsatile liver means pulsations felt over the liver which could be;

1. *Intrinsic pulsations due to;*
  - Tricuspid regurgitation (systolic pulsations) either organic or functional
  - Hemangioma of the liver
2. Transmitted pulsation from right ventricle due to
  - Right ventricular hypertrophy.

### *Method of Demonstration of Pulsations of Liver*

The presystolic or systolic pulsations of the heart can be transmitted to venous circulation in the liver in the presence of tricuspid incompetence, which can be detected as follows;

- Make the patient to sit in a chair, stand on the right side of the patient
- Place your right palm over liver in right hypochondrium and left palm over the back in the same manner as used for bimanual palpation.
- Ask the patient to hold his breath after taking deep inspiration
- Observed the lifting and separation of hands from the side with each heart beat.

In case of pulsatile liver, the hands are lifted and separated to some extent.

### *Clinical Tip*

In case of pulsatile liver, always look for other signs of tricuspid regurgitation (engorged pulsatile neck veins, v and y collapse and a pansystolic murmur) and congestive heart failure (cyanosis, dyspnoea, oedema).

### **171. What do you understand by the term liver span? What is its significance?**

**Ans.** The liver span is the vertical distance between the upper and lower borders of the liver which is defined either clinically (on percussion) or on ultrasound. Normal liver span in an adult is variable (10-14 cm), greater in men than in women, greater in tall people than in short.

### *Significance*

- Liver span is actually reduced when liver is small and shrunken (acute fulminant hepatitis) or masked when free air is present below the diaphragm as from a perforated viscus (liver dullness is masked, hence, span appears to be reduced).
- Liver span is increased when liver is enlarged not when liver is displaced.
- Serial observations may show a decreasing span of dullness with resolution of hepatitis, CHF or less commonly with progression of fulminant hepatitis.
- It is used to define actual vs apparent enlargement of liver.
  - Actual or real enlargement means palpable liver with increase in liver span.
  - Apparent enlargement means liver is palpable without being actually enlarged (liver span is normal). It is displaced downwards by right sided pleural effusion, pneumothorax, COPD or low diaphragm.

### **172. What is Reidle lobe of the liver?**

**Ans.** *Reidle' lobe of liver* is a tongue like projection of the right lobe of the liver, represents a variation in shape of the normal liver. It is commonly found in females or those with a lanky built. It is usually mistaken for a gall-bladder or right kidney, can be differentiated on ultrasound.

## CASE 15: PORTAL HYPERTENSION

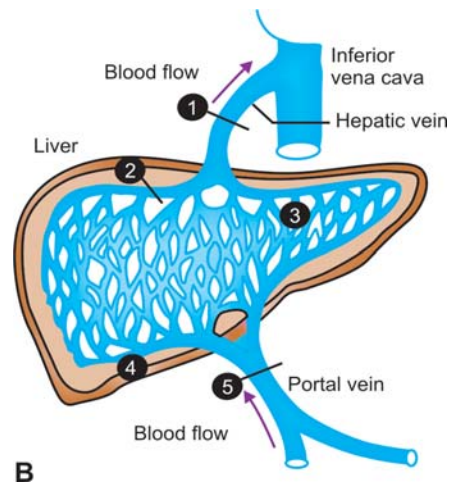
The patient (Fig. 1.15A) presented with distension of abdomen, weakness, dull abdominal ache and mild exertional dyspnoea for the last 3 months. There was history of haematemesis and jaundice in the past.

### Points to noted in the History

- History of fever, jaundice, bleeding from any site
- History of disturbance in consciousness, sleep or behavior problem
- Past history of alcoholism, drug intake, jaundice, delivery (in female)
- Family history of jaundice or similar illness
- Nutritional history.

### General Physical Examination

- Look for hepatic facies, e.g. earthy look, sunken (hollow) cheek and malar prominence—present in this case
- Assess nutritional status—poor in this case
- Look for stigmata of cirrhosis (wasting of muscles, palmar erythema, spider angiomas, testicular atrophy, gynecomastia, bilateral parotid enlargement and Dupuytren's contractures). Few stigmata were present.
- Look for signs of hepatic insufficiency, i.e. mental features, jaundice, bleeding (purpura, ecchymosis and bruising) clubbing of fingers, flapping tremors.
- Look for signs of portal hypertension, e.g. ascites, collaterals formation and fetor hepaticus, splenomegaly. Ascites and splenomegaly present.
- Look for anaemia, jaundice, Keyser-Fleischer's rings
- Look for signs of malnutrition and vitamin deficiency
- Look for peripheral pitting oedema. Which was present.
- Look for signs of CHF or pericardial effusion, e.g. raised JVP, cyanosis, neck pulsations etc.
- Note the vital signs, e.g. temperature, respiration, BP and pulse.



**Figs 1.15A and B:** A. Patient with symptoms and signs of portal hypertension due to cirrhosis of the liver.; B. Classification of portal hypertension depending on the site of obstruction

### Clinical Presentations

Patients usually present with;

- Progressive distension of abdomen, swelling of legs, haematemesis and melaena (e.g. portal hypertension)
- Fatigue, weight loss, flatulent dyspepsia, anorexia, malnutrition, muscle wasting drowsiness, disturbed sleep pattern (e.g. hepatic encephalopathy)

### Systemic Examination

#### Inspection

- Skin over the abdomen may be thin, shiny due to oedema of abdominal wall
- Abdominal distension with increased abdominal girth—present in this case.
- Prominent veins with flow of blood away from umbilicus
- Hernias (umbilical or inguinal) may or may not be present
- Umbilicus may be everted or transversely slit (smiling umbilicus) in presence of ascites (umbilicus was transversely slit in this case).

#### Palpation

- Liver was palpable, nontender, firm with sharp irregular margins. Left lobe was enlarged. In some cases, liver may not be palpable
- Spleen was also palpable, nontender, soft to firm
- Ascites was detected by fluid thrill
- Flow of blood in dilated veins was away from umbilicus.

Note: Palpate the liver and spleen by dipping method in presence of ascites.

#### Percussion

- Shifting dullness confirmed the presence of ascites
- Flanks were dull with central sparing
- Liver and splenic areas were dull.

#### Auscultation

Hear for;

- Bruit over liver. It indicates malignant liver
- Rub. It indicates perihepatitis due to infarction or may be heard over a nodule
- Venus hum around umbilicus. Its presence indicates portal hypertension (Cruveilhier-Bomgarten's syndrome)

**173. What is your clinical diagnosis and why?**

**Ans.** The clinical diagnosis is cirrhotic portal hypertension without hepatic encephalopathy. The points in favour are;

- Long history
- Past history of Jaundice and haematemesis
- Poor nutritional status e.g. shrunken cheeks
- Presence of stigmata of cirrhosis
- Presence of ascites, splenomegaly and collaterals with flow of blood away from umbilicus
- Pitting oedema.

**174. What is portal hypertension? How do the patients present with it?**

**Ans.** Normal portal venous pressure is low (5 to 10 mmHg) because vascular resistance in hepatic sinusoids is minimal. Portal hypertension is defined as elevated portal venous pressure more than 10 mmHg, results from increased resistance to portal blood flow. As the portal venous system lacks valves, therefore, obstruction at any level between right side of the heart and portal vein will result in retrograde transmission of elevated blood pressure.

Portal hypertension results in congestion of viscera (stomach and intestine), formation of collaterals and subsequent rupture, and precipitation of hepatic failure. Patient commonly presents with;

- Variceal bleeding, e.g. haematemesis; melaena, piles
- Chronic iron deficiency anaemia due to congestive gastropathy and repeated minor bleeding.
- Abdominal distension (ascites), splenomegaly.
- Spontaneous bacterial peritonitis.
- Symptoms and signs of hepatic encephalopathy (discussed below) may be associated with portal hypertension.
- Oliguria/anuria due to hepatorenal syndrome
- Hypersplenism leading to pancytopenia.

**175. How do you classify portal hypertension?**

**Ans.** Increased portal pressure can occur at three levels relative to hepatic sinusoids (Fig. 1.15B).

1. *Presinusoidal*. It means obstruction in the presinusoidal compartment outside the liver (between sinusoids and portal vein).
2. *Sinusoidal*. Obstruction occurs within the liver itself at the level of sinusoids.
3. *Postsinusoidal*. Obstruction is outside the liver at the

level of hepatic veins, inferior vena cava or beyond sinusoids within liver (veno-occlusive disease).

**176. What are the causes of portal hypertension?**

**Ans.** Cirrhosis is the most common cause, accounts for >90% of cases (Table 1.46).

**Table 1.46:** Causes of portal hypertension depending on the site of obstruction

- |   |
|---|
| <ol style="list-style-type: none"> <li>1. <b>Postsinusoidal</b> <ul style="list-style-type: none"> <li>• Extrahepatic postsinusoidal, e.g. Budd-Chiari syndrome</li> <li>• Intrahepatic postsinusoidal, e.g. veno-occlusive disease</li> </ul> </li> <li>2. <b>Sinusoidal</b> <ul style="list-style-type: none"> <li>• Cirrhosis of the liver</li> <li>• Cystic liver disease</li> <li>• Metastases in the liver</li> <li>• Nodular transformations of the liver</li> </ul> </li> <li>3. <b>Presinusoidal</b> <ul style="list-style-type: none"> <li>• <i>Intrahepatic presinusoidal</i>, e.g. schistosomiasis, sarcoidosis, congenital hepatic fibrosis, drugs and toxins, lymphoma, leukaemic infiltrations, primary biliary cirrhosis.</li> <li>• <i>Extrahepatic presinusoidal</i>, e.g. portal vein thrombosis, abdominal trauma, compression of portal vein at porta hepatis by malignant nodules or lymph node, pancreatitis.</li> </ul> </li> </ol> |
|---|

**177. Define noncirrhotic portal hypertension. What are its causes?**

**Ans.** This is defined as portal hypertension without hepatocellular damage and lack of nodular regeneration activity in the liver. These cases manifest usually with splenomegaly anaemia, recurrent variceal bleed and chances of hepatic encephalopathy are remote.

This disorder is usually associated with either congenital or acquired hepatic fibrosis, which may be localised or generalised. Some causes of noncirrhotic portal fibrosis are given in Table 1.47.

**Table 1.47:** Causes of noncirrhotic portal fibrosis

- |  |
|--|
| <ol style="list-style-type: none"> <li>1. <b>Idiopathic portal hypertension (noncirrhotic portal fibrosis, Banti's syndrome)</b> <ul style="list-style-type: none"> <li>• Intrahepatic fibrosis and phlebosclerosis</li> <li>• Portal and splenic vein sclerosis</li> <li>• Portal and splenic vein thrombosis</li> </ul> </li> <li>2. <b>Schistosomiasis</b> (pipe-stem fibrosis with presinusoidal portal hypertension)</li> <li>3. <b>Congenital hepatic fibrosis</b></li> <li>4. <b>Lymphomatous infiltration</b> around portal triad</li> </ol> |
|--|



**178. What are difference between cirrhotic and noncirrhotic portal hypertension?**

**Ans.** Differences between cirrhotic and noncirrhotic portal hypertension are given in the Table 1.48.

**Table 1.48:** Differentiation between cirrhotic and noncirrhotic portal-hypertension

Cirrhotic	Noncirrhotic
<ul style="list-style-type: none"> <li>• Slow insidious onset</li> <li>• Ascites present</li> <li>• Recurrent haematemesis uncommon</li> <li>• Anaemia moderate</li> <li>• Hepatic encephalopathy common</li> <li>• Oedema present</li> <li>• Liver biopsy shows cirrhosis</li> </ul>	<ul style="list-style-type: none"> <li>• Acute or sudden</li> <li>• Ascites absent</li> <li>• Recurrent haematemesis is common and presenting feature</li> <li>• Anaemia severe</li> <li>• Hepatic encephalopathy uncommon</li> <li>• No edema</li> <li>• No evidence of cirrhosis; only portal fibrosis seen</li> </ul>

**179. Define cirrhosis of the liver. What are its clinical characteristics?**

**Ans.** Cirrhosis is the pathological term, denotes irreversible destruction of liver cells (necrosis) followed by fibrosis and nodular regeneration of the liver cells in such a way that the normal liver architecture is lost.

*Clinical Features of Cirrhosis*

Cirrhosis may be totally asymptomatic, and in life time may be found incidentally at surgery or may just be associated with isolated hepatomegaly. The liver in cirrhosis may be large or small. When palpable, it is firm, nodular, nontender with sharp and irregular borders.

It may present with nonspecific complaints such as weakness, fatigue, muscle cramps, weight loss, nausea, vomiting, anorexia and abdominal discomfort.

The common clinical features of the cirrhosis are due to either liver cell failure with or without hepatic encephalopathy or portal hypertension.

**I. Signs of liver cell failure**

- *Hepatomegaly or small shrunken liver*
- *Jaundice, fever*
- *Circulatory changes, e.g. palmar erythema, spider angiomas, cyanosis (due to AV shunting in lungs), clubbing of the fingers, tachycardia, bounding pulses, hyperdynamic circulation.*

- *Endocrinal changes, e.g.*
  - Loss of libido, hair loss
  - Gynecomastia, testicular atrophy, impotence in males
  - Breast atrophy, irregular menses, amenorrhoea in females
- *Haemorrhagic manifestations, e.g.*
  - Bruises, epistaxis, purpura, menorrhagia
- *Miscellaneous*
  - Diffuse pigmentation
  - White nails
  - Dupuytren's contractures
  - Parotid enlargement.

**II. Signs of portal hypertension**

- *Splenomegaly*
- *Collateral vessels* formation at gastrooesophageal junction, around the umbilicus, behind the liver and in the rectum.
- *Vericeal bleeding* (haematemesis and malaena)
- *Fetor hepaticus* due to excretion of mercaptans in breath.

**III. Hepatic encephalopathy.** It comprises of features of liver cells failure described above plus mental feature described below;

- Mental features (e.g. reduced alertness, restlessness, behavioral changes, bizarre handwriting, disturbance in sleep rhythm, drowsiness, confusion, disorientation, yawning, and hiccups). In late stages, convulsions may occur and patient lapses into coma.

**180. What are precipitating factors for hepatic encephalopathy?**

**Ans.** There are certain factors that push the patient with compensated cirrhosis liver into decompensation phase (hepatic encephalopathy). These include;

- Drugs-like sedatives, hypnotics
- Gastrointestinal bleeding (e.g. varices, peptic ulcer, congestive gastropathy)
- Excessive protein intake
- Diuretics producing hypokalaemia and alkalosis
- Rapid removal of large amount of ascitic fluid in one setting (>3L)
- Acute alcoholic bout
- Constipation



- Infections and septicaemia, surgery
- Azotaemia (uraemia)
- Portosystemic shunts, e.g. spontaneous or surgical.

### 181. What is probable pathogenesis of hepatic encephalopathy?

**Ans.** Although, hepatic encephalopathy is called *ammonia encephalopathy* but  $\text{NH}_3$  is not only the culprit. The possible mechanisms are;

- Increased  $\text{NH}_3$  levels in blood
- Increased levels of short-chain fatty acids
- Increase in false neurotransmitters like octopamine and rise in GABA level (true neurotransmitter)
- Rise in methionine levels
- Rise in certain amino acids (ratio of aromatic amino acids to branched chain amino acid is increased).

All these products described above are retained in blood in higher concentration due to combined effect of liver cell failure (decreased metabolism) and portosystemic shunting (delivery of these substances into circulation by bypassing the liver).

### 182. How do you stage/grade the hepatic encephalopathy?

**Ans.** Clinical staging of hepatic encephalopathy is important in following the course of illness and to plan the treatment as well as to assess the response to therapy (Table 1.49).

**Table 1.49:** Clinical staging of hepatic encephalopathy

Stage	Mental features	Tremors	EEG change
I	Euphoria or depression, confusion, disorientation, disturbance of speech and sleep pattern	+/-	Normal EEG
II	Lethargy, moderate confusion	+	High voltage triphasic slow waves (abnormal EEG)
III	Marked confusion, incoherent speech, drowsy but arousable	+	High voltage Triphasic waves (2-5/sec) (abnormal EEG)
IV	Coma, initially responsive to noxious stimuli, later unresponsive	-	Delta activity (abnormal EEG)

### 183. What are diagnostic criteria for hepatic encephalopathy?

**Ans.** The four major criteria are:

1. Evidence of acute or chronic hepatocellular disease with extensive portosystemic collaterals
2. Slowly deterioration of consciousness from reduced awareness to confusion, disorientation, drowsiness or stupor and finally into coma.
3. Shifting combination of neurological signs including asterix (tremors), rigidity, hyper-reflexia, extensor plantar response and rarely seizures.
4. EEG changes. Symmetric high voltage triphasic waves changing to delta slow activity.

### 184. What will you look on general physical examination in a patient with cirrhosis of the liver?

**Ans.** Examination of a patient with cirrhosis is as follows: (Read case summary also in the beginning)

#### General Physical Signs

Look for;

- Malnutrition, vitamin deficiency
- Anaemia
- Jaundice (icterus)
- Hepatic facies, e.g. earthy look, shunken shiny eye balls, muddy facial expression, sunken cheeks with malar prominence, pinched up nose and parched lips, icteric tinge of conjunctiva
- Oedema feet
- Obvious swelling of abdomen
- Wasting of muscles
- Foul smell (feto hepaticus)
- Flapping tremors
- Keyser-Fleischer's ring
- Cyanosis.

#### Skin Changes

Look for the followings;

- Spider naevi
- Pigmentation of skin
- Gynaecomastia and testicular atrophy in males
- Palmar erythema
- Scanty axillary and pubic hair in male, breast atrophy in females

- White nails
- Dupuytren's contracture.

### 185. What are complications of cirrhosis?

**Ans.** Followings are complications:

- Portal hypertension (fatal variceal bleeding)
- Hepatocellular failure and subsequent hepatic encephalopathy
- Spontaneous bacterial peritonitis
- Septicaemia
- Increased incidence of peptic ulcer and hepatocellular carcinoma
- Nutritional debility (e.g. anaemia, hypoproteinaemia)
- Hepatorenal syndrome. It is functional acute renal failure in a patient with cirrhosis of the liver, develops due to circulatory or haemodynamic changes. The exact aetiology is unknown. The kidneys structurally are normal but functionally abnormal, hence called *functional renal failure*. The prognosis is poor. Hepatorenal syndrome rarely can develop in hepatitis also.
- Haemorrhagic tendency.

### 186. What are the causes of death in cirrhosis?

**Ans.** Common causes are as follows:

1. Most common cause is fatal septicaemia (gram-negative)
2. Hepatic encephalopathy
3. Cerebral oedema
4. Fatal bleeding
5. Renal failure (hepatorenal syndrome)
6. Hypoglycaemia, hypokalaemia etc.

### 187. What are causes of upper GI bleed in cirrhosis of liver?

**Ans.** The causes are:

1. Oesophageal varices
2. Gastric varices/erosions
3. Congestive gastropathy
4. Gastroduodenal ulcerations
5. Mallory-Weiss tear
6. Bleeding tendencies

### 188. How will you investigate a case with cirrhosis of the liver?

**Ans.** Investigations of cirrhosis are as follows:

#### 1. Complete haemogram and ESR, may show:

- **Anaemia.** Anaemia in cirrhosis is due to haematemesis, malaena, anorexia with poor intake of nutrients, piles, malabsorption and hypersplenism. Anaemia is commonly microcytic and hypochromic.
- Pancytopenia (anaemia, leucopenia and thrombocytopenia) is due to hypersplenism.
- Raised ESR indicates infections.

#### 2. Stool for occult blood (Guaiac test) may be positive. Bleeding in cirrhosis is intermittent, hence, test may be performed at least for 3 consecutive days. Vitamin C intake may give false positive result.

#### 3. Rectal examination for internal piles

#### 4. Chest X-ray for lung pathology or pleural effusion

#### 5. Hepatic profile

- Total serum proteins and albumin may be low. The albumin/ globulin ratio is altered.
- Serum bilirubin is normal or raised
- Serum transaminases are normal or mildly elevated
- Alkaline phosphatase is mildly elevated
- Serum cholesterol is low
- Prothrombin time is normal or increased and does not return to normal with vitamin K therapy. Low PT is bad prognostic sign
- Viral markers (HbAg) are negative
- Serum autoantibodies, antinuclear, anti-smooth muscle and antimitochondrial antibodies level increase in autoimmune hepatitis, cryptogenic cirrhosis and biliary cirrhosis.
- Serum immunoglobulins, e.g. IgG is increased in autoimmune hepatitis, IgA increased in alcoholic cirrhosis and IgM in primary biliary cirrhosis.

#### 6. Other blood tests, e.g. serum copper (Wilson's disease), iron (haemochromatosis), serum alpha-1-antitrypsin (cystic fibrosis) and serum alpha-fetoprotein (hepatocellular carcinoma).

#### 7. Imaging

- Ultrasound for liver may reveal change in size, shape and echotexture of the liver. Fatty change and fibrosis produce diffuse increased echogenicity. The presence of ascites, portal vein

diameter ( $>14$  mm indicates portal hypertension), presence of varices and splenomegaly can be determined on USG.

- Barium swallow for oesophageal varices (worm-eaten appearance due to multiple filling defects).
- CT scan is not better than USG in cirrhosis of liver.

**8. Upper GI endoscopy** shows oesophageal and gastric varices, peptic ulcer or congestive gastropathy (petechial haemorrhages both old and new, seen in gastric mucosa- mosaic pattern of red and yellow mucosa).

**9. Pressure measurement studies**

- Percutaneous intrasplenic pressure is increased in portal hypertension.
- Wedged hepatic venous pressure is increased.

**10. Dynamic flow studies.** These may show distortion of hepatic vasculature or portal vein thrombosis

- Doppler ultrasound for visualisation of portal venous system and duplex Doppler for measurement of portal blood flow.
- Portal venography by digital subtraction angiography.

**11. Electroencephalogram (EEG)** may show triphasic pattern in hepatic encephalopathy.

**12. Liver biopsy.** It is a gold standard test to confirm the diagnosis of cirrhosis and helps to find out its cause. Special stains can be done for iron and copper.

**13. Tapping of the ascites.** Ascites is transudative (serum albumin/ascites albumin gradient  $> 1.1$ ). The fluid should be sent for cytology, biochemistry and for culture if bacterial peritonitis is suspected.

## CASE 16: CHRONIC DIARRHOEA AND MALABSORPTION

The 14 years male adolescent (Fig. 1.16) was brought by the mother with complaints of stunted growth and reduction in weight. There was history of chronic diarrhoea since childhood. There was history of intermittent loose motion since then.

### Points to be Noted in History

- History of fever, worm expulsion or recurrent episodes of diarrhoea
- Any relation of diarrhoea with food or milk
- History of oedema feet, distension of abdomen
- Developmental history including milestones
- Nutritional history
- Family history

### General Physical Examination

- Record height and weight, and calculate BMI
- General appearance, e.g. facial puffiness, protuberant abdomen
- Look for deficiency signs of nutrients e.g. protein (weakness, muscle wasting, flabbiness, oedema, protuberant abdomen, thin-peppary skin), fat (thin extremities, sunken cheeks, flat buttocks and thin chest, etc.
- Look for signs of vitamin deficiency, e.g. xerosis, bitot's spots, cheilosis, angular stomatitis, spongy and bleeding gums, bowing of the legs, rickety rosary, purpuric or ecchymotic patches, peripheral neuropathy and anaemia
- Record pulse, BP, temperature and respiration
- Look for lymphadenopathy any where in the body e.g. neck, axilla, groin, etc.



**Fig. 1.16:** An adolescent with stunted growth and chronic diarrhoea. There was anaemia, oedema feet of a signs of multiple nutrient deficiency.

### Clinical Presentations (Fig. 1.16)

These patients present with;

1. Passage of loose stools >3 per day for the last 3 months.
2. Patients may complain of nonspecific symptoms, e.g. ill health, weakness, fatigue, weight loss with signs and symptoms of malnutrition, anaemia, vitamins and mineral deficiency.
3. Specific symptoms and signs depending on the underlying cause;
  - Fever, pain abdomen, diarrhoea with or without blood may suggest underlying inflammatory bowel disease.
  - Presence of oedema face and feet, anaemia, muscle wasting and weight loss indicate hypoproteinaemia due to protein-losing enteropathy.
  - The presence of steatorrhea (large, offensive stools with increased fat content) indicates either pancreatic or hepatic cause of malabsorption.
  - Diarrhoea with features of Vit. B<sub>12</sub> deficiency (red tongue- glossitis, macrocytic anaemia, peripheral neuropathy and subacute combined degeneration of the cord) indicate chronic gastritis or malabsorption due to involvement of terminal ileum (site of vit. B<sub>12</sub> absorption) due to any cause or bacterial proliferation in blind loop syndrome or stricture of bowel.
  - Diarrhoea following ingestion of milk or milk products indicate milk allergy or lactose intolerance.

### Systemic Examinations

All the major systems have to be examined.

#### I. Abdomen

- Note abdominal protuberance flabby abdominal muscle and oedema of abdominal wall
- Look for the signs of ascites due to hypoproteinaemia
- Look for enlargement of spleen, liver due to anaemia or inter-current infection
- Look for any abdominal lymph nodes.

#### II. CVS Examination

- Examine the heart for any enlargement, murmur, rub or abnormal sound

#### III. Examination of nervous system

- Look for evidence of beri-beri, Korsakoff Wernicke's encephalopathy, peripheral neuropathy or mental subnormality

#### IV. Endocrine and metabolism

- Look for signs of hypopituitarism, hypothyroidism, rickets

#### V. Other systems

- Respiratory system for any evidence of tuberculosis or infection
- Skin for any dryness, bleeding etc
- Joints.
- Haematopoietic system for anaemia, bleeding.

**189. What is probable diagnosis of the patient in picture?**

**Ans.** In an adolescent child with diarrhoea since childhood, reduced weight and height, history of delayed milestones, presence of anaemia, protuberant abdomen, muscle wasting, oedema feet, signs of multiple nutrients and vitamins deficiency, the clinical diagnosis of malabsorption syndrome is most likely.

**190. How do you define diarrhoea?**

**Ans.** Diarrhoea is defined as passage of frequent loose stools, i.e. more than 3 in a day. Quantitatively it is defined as faecal output >200 mg/day when dietary fibre content is low.

Acute diarrhoea means rapid onset of diarrhoea occurring in an otherwise healthy person not lasting for more than 2 weeks. It is usually infective in origin (viral or bacterial).

Chronic diarrhoea refers to slow onset of diarrhoea persisting for more than 3 months. It is usually a symptom of some underlying disease or malabsorption syndrome.

*Malabsorption syndrome* refers to defective absorption of one or more essential nutrients through the intestine. The malabsorption may be specific or generalised. The examples of specific malabsorption include lactose intolerance, vitamin B<sub>12</sub> malabsorption etc.

**191. What are causes of malabsorption?**

**Ans.** Malabsorption may be due to diseases of pancreas, GI tract and the liver. The causes of malabsorption are given in Table 1.50.

**192. What are the common causes of chronic diarrhoea?**

**Ans.** The causes are:

- Inflammatory bowel disease, e.g. ulcerative colitis, Crohn's disease
- Coeliac disease (gluten-induced) or tropical sprue
- Intestinal diseases, e.g. tuberculosis, stricture, fistula
- Worm infestations, e.g. giardiasis
- Pancreatic disease, e.g. chronic pancreatitis, malignancy
- Endocrinal causes, e.g. diabetes, Addison's disease, thyrotoxicosis, etc.

**193. How will you investigate a case of malabsorption?**

**Ans.** The various tests of malabsorption of different nutrients are enlisted in Table 1.51.

**Table 1.50:** Causes of malabsorption syndrome

<b>A. Pancreatic disorders (disorders of maldigestion)</b>	
1.	Chronic pancreatitis
2.	Cystic fibrosis
3.	Malignancy pancreas
4.	Ulcerogenic tumours of pancreas (Zollinger-Ellison's syndrome)
<b>B. Disorders causing deficiency of bile acids/bile salts</b>	
<b>1. Interruption of enterohepatic circulation of bile acids/salts or reduced bile salt concentration.</b>	
a.	Ileal resection or inflammatory bowel disease
b.	Parenchymal liver disease or cholestasis (intra or extrahepatic)
<b>2. Abnormal bacterial proliferation in small intestine leading to bile salt deconjugation</b>	
a.	Blind loop (stagnant loop) syndrome
b.	Strictures or fistulas of small intestine
c.	Hypomotility of small intestine due to diabetes
<b>3. Drugs causing sequestration or precipitation of bile salts, e.g. neomycin and cholestyramine</b>	
<b>4. Inadequate absorptive surface</b>	
a.	Intestinal resection or bypass surgery of intestine.
<b>5. Mucosal defects of absorption (inflammatory, infiltrative or infective disorders)</b>	
a.	Tropical sprue .
b.	Lymphoma
c.	Whipple's disease
d.	Radiation enteritis
e.	Amyloidosis
f.	Giardiasis
g.	Scleroderma
h.	Eosinophilic enteritis
i.	Dermatitis herpetiformis
<b>C. Biochemical or genetic abnormalities</b>	
1.	Coeliac disease (gluten-induced enteropathy)
2.	Disaccharidase deficiency
3.	Hypogammaglobulinaemia
4.	Abetalipoproteinaemia
<b>D. Endocrinal or metabolic defects</b>	
a.	Diabetes mellitus
b.	Addison's disease
c.	Carcinoid syndrome
d.	Hyperthyroidism
<b>E. Specific malabsorption (mucosa is histologically normal)</b>	
a.	Lactase deficiency
b.	Vitamin B <sub>12</sub> malabsorption

**194. How will you diagnose malabsorption?**

**Ans.** Diagnosis of malabsorption is based on:

1. Symptoms and signs suggestive of malabsorption (diarrhoea >3 months with deficiency signs of one or more nutrients).



Table 1.51: Investigations for malabsorption

Test	Normal values	Malabsorption (non-tropical sprue)	Maldigestion (pancreatic insufficiency)
<b>I. Fat absorption</b>			
1. Faecal fat (24 hours excretion)	< 6.0 g/day	> 6.0 g/day	>6.0 g/day
2. Fat in stools (%)	< 6	< 9.5 and > 6	>9.5 (steatorrhoea)
<b>II. Carbohydrate absorption</b>			
1. D-xylose absorption (25.0 g oral dose)	5 hours urinary excretion >4.5 g	Decreased	Normal
2. Hydrogen breath test (oral 50.0 gm lactose and breath H <sub>2</sub> measured every hour for 4 hours)	Less than 10 ppm above baseline in any sample	Increased	Normal
<b>III. Protein absorption</b>			
1. Faecal clearance of endogenous alpha-1 antitrypsin measured in three days collection of stools	Absent in stools	Increased	Increased
2. Nitrogen excretion (3-5 days collection of stools)	< 2.5 g/day	>2.5 g/day	>2.5 g/day
<b>IV. Vitamins absorption</b>			
1. Radioactive B <sub>12</sub> absorption test (0.5 µg of labelled Vit. B <sub>12</sub> is given orally followed 2 hrs later by 1000 µg of non-labelled B <sub>12</sub> given by IM injection. Radioactivity in the urine is seen after 24 hours)	>16% radioactivity in urine	Frequently decreased	Frequently decreased
<b>V. Other tests</b>			
1. <i>Breath tests</i>			
a. Breath <sup>14</sup> CO <sub>2</sub> ( <sup>14</sup> C xylose)	Minimal amount	Decreased	Normal
b. Bile salt breath test (radioactive)	< 1% dose excreted <sup>14</sup> CO <sub>2</sub> in 4 hrs	Normal	Normal
2. <i>Blood tests</i>			
a. Serum calcium	9-11 mg/dl	Frequently decreased	Normal
b. Serum albumin	3.5-5.5 g/dl	Frequently decreased	Normal
c. Serum iron	80-150 µg/dl	Decreased	Normal
d. Serum vit. A	>100 IU/dl	Decreased	Decreased
<b>VI. Miscellaneous</b>			
1. Bacterial (culture)	<10 <sup>5</sup> organisms/ml	Normal but abnormal in blind loop syndrome	Normal
2. Secretin test	Volume (1.8 ml/kg/hr) and bicarbonate (>80 mmol/L) Concentration in duodenal aspirate	Normal	Abnormal
3. Barium study (follow through)	Normal pattern	Flocculations and segmentations of barium column (malabsorption pattern –see text)	Normal pattern
4. Small intestine biopsy	Normal mucosa	Abnormal	Normal

2. Biochemical tests or other investigations documenting the evidence of malabsorption to one or more nutrients.
3. Radiology of small intestine may show either gastrointestinal motility disorder, fistula, stricture, Zollinger-Ellison's syndrome or characteristic intestinal changes of malabsorption, i.e. breaking up of barium column with segmentation, clumping and coarsening of mucosal folds (*Moulage's sign*).
4. Biopsy and histopathology of small intestine shows partial villous atrophy with lymphocytic infiltration.

### 195. What are diagnostic criteria for nontropical sprue?

**Ans.** Diagnostic clues to nontropical sprue (coeliac disease) are given in Table 1.52.

**Table 1.52:** Diagnostic criteria for nontropical sprue

1. Clinical	Symptoms and signs of long duration suggestive of malabsorption (Table 1.61)
2. Biochemical	Positive evidence of fat, carbohydrate, protein, vit. B <sub>12</sub> , folate malabsorption (Table 1.59)
3. Immunological	Antigliadin, antireticulin and antiendomysial antibodies are seen in high titres in majority of patients
4. Histopathology of small intestine	Villous or subvillous atrophy with mononuclear cells infiltration of lamina propria and submucosa
5. Therapeutic response	Clinical, biochemical and histopathological improvement on gluten-free diet

### 196. What are symptoms and signs of malabsorption syndrome?

**Ans.** Due to fecal loss of certain nutrients, vitamins and minerals, their deficiency symptoms and signs appear (Table 1.53).

### 197. What is Traveller's diarrhoea?

**Ans.** It is an acute infective diarrhoea frequently seen in tourists caused by the following pathogenic organisms;

- Enterotoxigenic *E. coli*
- Shigella
- Salmonella
- Campylobacter

**Table 1.53:** Deficiency signs in malabsorption syndrome

Deficiency	Signs and symptoms
Vitamin A	• Night blindness, xerosis, Bitot's spots, keratomalacia, dryness of eyes and follicular hyperkeratosis of skin
Vitamin C	• Scurvy
Vitamin D	• Rickets in children and osteomalacia in adults
Vit. K	• Bleeding tendencies
Vitamin B complex	• Bald tongue, angular cheilosis, stomatitis, glossitis, peripheral neuropathy, subacute combined degeneration, megaloblastic anaemia, dermatitis and dementia (pellagra)
Deficiency of nutrients (carbohydrate, proteins, fats)	• Vague ill health, fatigue, weight loss
Iron deficiency	• Muscle wasting and oedema
Calcium deficiency	• Anaemia
Potassium deficiency	• Bone pain, tetany, paraesthesias, muscle wasting
Sodium and water depletion	• Distension of abdomen, diminished bowel sounds, vomiting, muscle weakness and EKG changes
	• Nocturia, hypotension

- Rota virus
- Giardia intestinal, *Entamoeba histolytica*.

It is characterised by sudden onset of diarrhoea with watery stools, fever, nausea, vomiting, abdominal pain which lasts for 2-3 days. On examination, there may be diffuse tenderness of abdomen. Treatment is tetracycline or ciprofloxacin *plus* metronidazole combination with correction of dehydration.

### 198. What is pseudomembranous colitis?

**Ans.** It is an antibiotic-induced diarrhoea caused by an opportunistic commensal *clostridium difficile*. It can occur in immunocompromised state also. The antibiotics incriminated are: ampicillin, clindamycin and cephalosporins.

### 199. What is spurious diarrhoea?

**Ans.** It occurs following faecal impaction in constipated patients, seen in old persons, characterised by sense of incomplete evacuation and gaseous distension with diarrhoea. It is relieved by enema.

**200. What do you know about blind-loop syndrome? What are its causes?**

**Ans.** The term refers to small intestinal abnormality associated with outgrowth of bacteria (bacterial count is  $>10^8$ /ml) causing steatorrhoea, and vitamin B<sub>12</sub> malabsorption, both of which improve dramatically after oral antibiotic therapy. This also called “contaminated bowel syndrome”, or “small intestinal stasis syndrome”.

Normally the small intestine is either sterile or contain  $< 10^4$  organism/ml.

The **causes** are:

- Gastric surgery
- Diverticulosis
- Fistulae
- Bowel resection
- Diabetic autonomic neuropathy
- Hypogammaglobulinemia.

All these structural abnormalities lead to delivery of the coliform bacteria from colon to small intestine and predispose to their proliferation.

The triphasic malabsorption test for vitamin B<sub>12</sub> as detailed below is diagnostic.

Stage I. Malabsorption without replacement of intrinsic factor

Stage 2. Malabsorption persists with replacement of intrinsic factor

Stage 3. Malabsorption to B<sub>12</sub> improves after a 5-7 days course of antibiotic therapy.

**201. What is lactose intolerance?**

**Ans.** It occurs due to deficiency of an enzyme *lactase* – a disaccharidase which normally hydrolyses lactose to glucose and galactose. The deficiency may be primary (inherited) or secondary (acquired), is characterised by abdominal colic, distension of abdomen and increased flatus followed by diarrhoea on ingestion of milk; withdrawal or substitution therapy with enzyme *lactase* improves the condition.

**202. What do you understand by the term protein-losing enteropathy?**

**Ans.** The term implies excessive loss of proteins through the GI tract leading to hypoproteinaemia and its clinical manifestations such as oedema face and feet, muscle wasting (flabbiness of muscles) and weight loss.

A variety of disorders lead to it (Table 1.54).

**Table 1.54:** Disorders producing protein-losing enteropathy

**1. Disorders of stomach**

- a. Hypertrophic gastritis (Menetrier’s disease)
- b. Gastric tumours

**2. Disorders of intestine**

- a. Intestinal lymphangiectasia
- b. Whipple’s disease
- c. Tropical sprue
- d. Coeliac disease (nontropical sprue)
- e. Intestinal tuberculosis
- f. Parasitic infections
- g. Lymphoma
- h. Allergic gastroenteropathy
- i. Inflammatory bowel disease, e.g. regional enteritis

**3. Cardiac disorders**

- a. Congestive heart failure
- b. Constrictive pericarditis

The diagnosis of protein-losing enteropathy is confirmed by measurement of fecal nitrogen content (increased) and fecal clearance of alpha-1-antitrypsin or <sup>51</sup>Cr labelled albumin after I.V. injection. Excessive intestinal clearance of alpha-1-antitrypsin  $>13$  ml/day (normal  $<13$  ml/day) confirms the diagnosis.

**203. What is the difference between food intolerance and food allergy?**

**Ans.** *Food intolerance* is an adverse reaction to food. It is not immune-mediated and results from a wide range of mechanisms such as contaminants in food, preservatives and lactase deficiency etc.

*Food allergy* is an immune-mediated disorder due to IgE antibodies and type I hypersensitivity reaction to food. The most common food associated with allergy are; milk, egg, soya bean and shellfish. Food allergy may manifest as:

- *Oral allergy syndrome*—contact with certain fruit juices results in urticaria and angioedema of lips and oropharynx.
- *Allergic gastroenteropathy* leading to diarrhoea with discharge of eosinophils in the stools.
- *Gastrointestinal anaphylaxis* leading to nausea, vomiting, diarrhoea, and sometimes cardiovascular or respiratory collapse.
- Diagnosis is confirmed by double-blind placebo-controlled food challenges.

**Table 1.55:** Clinical features of two common inflammatory bowel disorders

Features	Crohn's disease	Ulcerative colitis
Presenting symptoms	Diarrhoea and pain abdomen in right lower quadrant with tenderness and guarding	Diarrhoea with blood, mucus and pus. Pain in left lower abdomen and fever may be present. Tenderness in left side of abdomen or left iliac fossa
Palpation	A mass may be palpable on abdominal and/or rectal examination. It is an inflammatory mass	No mass palpable
Colics/diffuse pain	Recurrent abdominal colics are common due to obstruction	No colicky pain. Toxic megacolon may produce diffuse pain associated with distension of abdomen and stoppage of loose motions
Signs and symptoms of malabsorption	Moderate diarrhoea and fever. Stools are loose or well formed. Features of malabsorption of fat, carbohydrate, protein, Vit. D and Vit. B <sub>12</sub> are common. These patients have anaemia, weight loss, growth retardation (in children)	Patients have severe diarrhoea with tenesmus. Anaemia, weight loss present. Malabsorptive features are less common but dehydration common
Relapses or remissions	Common	Common
Stricture/anal fissure	Common	Less common
Abscess and fistulas	Common	Less common
Carcinoma in situ	Less common	More common in long-standing disease
Systemic involvement (hepatic, ocular, skin, ankylosing spondylitis, arthritis)	Less common	More common

**Note:** These distinctions in clinical features are arbitrary and should not be interpreted in absolute sense.

#### 204. What are inflammatory bowel disorders?

**Ans.** These are nonspecific inflammatory disorders of bowel having similar aetiopathogenesis, pathology, investigations, complications and treatment. Exact causes of these disorders are unknown. Two common disorders are:

- Crohn's disease
- Ulcerative colitis

The clinical characteristics of both these disorders are compared in Table 1.55.

## CASE 17: ACUTE NEPHRITIC SYNDROME

The female patient (Fig. 1.17A) presented with pain abdomen, puffiness of face and passed dark coloured small amount of urine < 400 ml (Fig. 1.17B). The followed an episode of fever for 3 weeks.

### Points to be noted in history

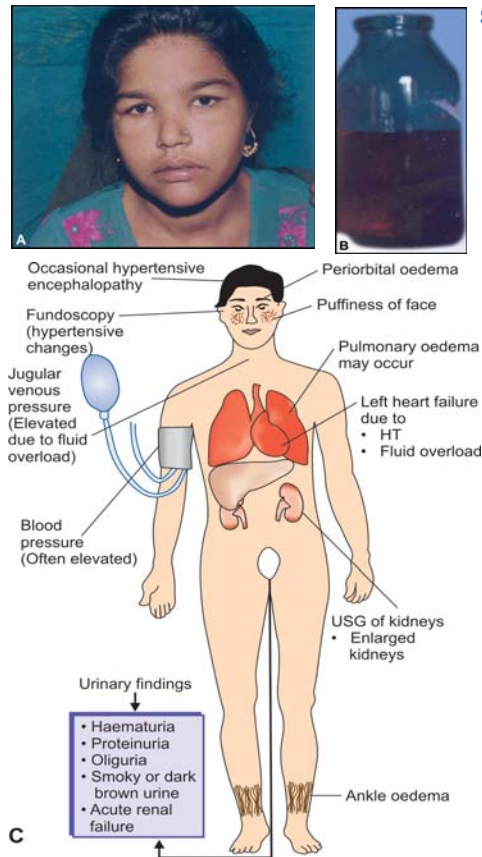
#### Age

- The patient is usually a child or adolescent
- Ask for the following;
- History of fever, sore throat, tonsillitis, pharyngitis, otitis media or cellulitis
- History of collagen vascular disorder or a haematological disorder
- History of vaccination (DPT)
- History of oliguria, puffiness of face, change in colour of urine
- H/O drug rash, jaundice breathlessness, headache and oedema feet
- History of disturbance in consciousness, luzziness, lethargy, nausea, vomiting, pruritus, palpitation (features of uraemia).

### General physical examination

#### Look for

- Face (periorbital oedema, puffiness present)
- Pulse and BP (BP is high)
- JVP: It is raised
- Oedema feet, sacral oedema present
- Note the change in colour of urine (red, brown, or smoky).



**Figs 1.17A to C:** A: A young female patient having puffiness of face. B: 24 hour Urine of the patient which is small in amount smoky and shows RBCs and proteinuria. C: Clinical manifestations of acute nephritic syndrome (diagram)

### Clinical Presentations

- The patients usually children or young adults present with the complaints of puffiness of face especially around the eyes in the early hours of the morning on getting out of bed (Fig. 1.17A).
- They may complain of reduced urine output or change in colouration of the urine (Fig. 1.17B).
- They may complain of headache, fatigue, weakness, breathlessness, cough, haemoptysis due to hypertension or left heart failure.
- Sometimes they may present with symptoms and signs of underlying disease.
- Sometimes they may present with fractures of hypertensive encephalopathy (mental changes, headache seizures) or uraemia (GI symptoms or ill health).

### Systemic Examinations

- Examination of CVS**
  - Look for the signs of cardiomegaly. Auscultate the heart for any murmur or rub or abnormal sound (3rd heart sound)
- Examination of lungs**
  - Auscultate the lungs for crackles or rales for fluid overload or noncardiogenic pulmonary oedema due to LVF
- Examination of abdomen**
  - Inspect the abdomen for distension or ascites
  - Elicit the signs for presence of ascites or oedema of abdominal wall
  - Palpate the abdomen for any organ enlargement
- Examination of CNS**
  - Note the features of hypertensive-encephalopathy
  - Fundoscopy



**205. What is the clinical diagnosis of the patient in picture?**

**Ans.** The young female patient presenting with morning puffiness of face, oliguria, smoky urine and hypertension probably has acute nephritic syndrome as the first possibility due to any cause.

**206. How do you define acute nephritic syndrome?**

**Ans.** *Acute nephritic syndrome* is characterised by an acute transient inflammatory process involving mainly the glomeruli and to lesser extent the tubules, manifests clinically with oliguria, hypertension, haematuria, oedema and rapid renal failure. Acute glomerulonephritis (AGN) is interchangeably used as acute nephritic syndrome.

The term *rapidly proliferative glomerulonephritis* (RPGN) is used for those patients of AGN who do not go into remissions, spontaneously develop acute renal failure over a period of weeks to months. These patients belong to either a primary glomerular disease or a complicating multisystem disease (secondary glomerular disease).

**207. What are clinical hallmark of acute nephritic syndrome and what is their pathogenesis?**

**Ans.** The clinical hallmarks of acute nephritic syndrome are depicted in Figure 1.17C. Their pathogenesis is given in the box.

**ACUTE NEPHRITIC SYNDROME**

Feature	Mechanism (Cause)
• Early morning puffiness or periorbital oedema	• Collection of fluid in loose periorbital tissue
• Haematuria (gross or microscopic)	• Glomerular inflammation
• Hypertension	• Retention of Na and H <sub>2</sub> O
• Oedema	• Retention of salt, H <sub>2</sub> O and hypertension
• Uraemia	• Retention of urea and creatinine
• Oliguria	• Reduced GFR

**208. What is its etiopathogenesis?**

**Ans.** It is an immune complex glomerulonephritis characterised by production of antibodies against glomerular antigen, deposition of immune complexes

in the walls of glomerular capillaries which modify the immune system leading to inflammation of the glomeruli. The stepwise pathogenesis is given in Table 1.56.

**Table 1.56:** Stepwise pathogenesis of nephritic syndrome

1. *Binding of antibodies* directed against glomerular basement membrane antigen
2. *Trapping* of soluble immune complexes in the glomerular capillary wall (subepithelial or sub-endothelial).
3. *In situ immune complex formation* between circulating antibody and fixed antigen or antigen planted either in the mesangium and/ or in capillary wall.
4. *Action of circulating primed T cells* with macrophages.

**209. What are causes of acute nephritic syndrome?**

**Ans.** All the causes that lead to acute glomerular injury may lead to acute nephritic syndrome (Table 1.57).

**Table 1.57:** Causes of AGN (acute nephritic syndrome)**I. Infectious diseases**

- a. Post-streptococcal glomerulonephritis
- b. Non-streptococcal glomerulonephritis
  - i. Bacterial: Infective endocarditis staphylococcal and pneumococcal infection, typhoid, syphilis and meningococcaemia
  - ii. Viral: Hepatitis B, infectious mononucleosis, mumps, measles, coxsackie and echoviruses
  - iii. Parasitic – malaria

**II. Systemic disorders**

Systemic lupus erythematosus (SLE), Vasculitis, Henoch-Schonlein purpura, Goodpasture's syndrome

**III. Primary glomerular diseases**

Mesangiocapillary glomerulonephritis, mesangial proliferative glomerulonephritis

**IV. Miscellaneous**

Guillain-Barre syndrome, serum sickness, DPT vaccination, IgA nephropathy

**210. What are the causes of rapidly proliferative glomerulonephritis (RPGN)?**

**Ans.** It is a complication of acute glomerulonephritis or a manifestations of a multisystem disease (Table 1.58). The clinical features are summarised in Table 1.59.

**211. Enumerate the complications of acute nephritic syndrome.**

**Ans.** Complications are either due to retention of salt and water (volume overload) or hypertension or capillaritis. These include;

- Fluid overload

**Table 1.58:** Causes of RPGN

<b>I. Infectious diseases</b>
a. Poststreptococcal glomerulonephritis
b. Infective endocarditis
<b>II. Multisystem diseases</b>
a. Systemic lupus erythematosus (SLE)
b. Goodpasture's syndrome
c. Vasculitis
d. Henoch-Schonlein purpura
<b>III. Primary glomerular disease</b>
a. Idiopathic
b. Mesangiocapillary glomerulonephritis
c. Membranous glomerulonephritis (anti-glomerular basement membrane antibodies nephritis)

**Table 1.59:** Clinical manifestations of rapidly proliferative glomerulonephritis

<b>1. Signs and symptoms of azotemia</b>
Nausea, vomiting, weakness. The azotemia develops early and progresses faster.
<b>2. Signs and symptoms of acute glomerulonephritis</b>
It includes oliguria, abdominal flank pain due to large kidneys, haematuria, hypertension and proteinuria

- Hypertensive encephalopathy
- Acute left heart failure
- Noncardiogenic pulmonary oedema
- Rapidly progressive glomerulonephritis (RPGN)

**Table 1.60:** Investigations of acute nephritic syndrome

<i>Investigation</i>	<i>Positive finding</i>
1. Urine microscopy	1. RBCs and red cell casts
2. Urine complete	2. High Sp. gravity, proteinuria present
3. Blood urea and serum creatinine	3. May be elevated
4. Culture (throat swab, discharge from ear, swab from infected skin)	4. Nephrogenic streptococci – not always
5. ASO titre	5. Elevated in post-streptococcal nephritis
6. C3 level	6. Reduced
7. Antinuclear antibody (ANA)	7. Present in significant titres in lupus (SLE) nephritis
8. X-ray chest	8. Cardiomegaly, pulmonary oedema – not always
9. Renal imaging (Ultrasound)	9. Usually normal or large kidneys
10. Renal biopsy	10. Glomerulonephritis

- Uraemia
- Massive hemoptysis

## 212. How will you proceed to investigate a patient with acute nephritic syndrome?

**Ans.** The investigations to be done are given in Table 1.60.

**CASE 18: NEPHROTIC SYNDROME**

A-18-year male (Fig. 1.18) presented with complaints of puffiness of face in the morning, oedema feet and distension of the abdomen for the last 1 year. Patient is passing normal amount of urine of normal colour. There is no history of headache, blurring of vision, dizziness, breathlessness or orthopnoea nausea, vomiting. There is no history of disturbance in consciousness.

**Points to be noted in the history**

Ask the followings on history;

- Symptoms, their duration, progression, relapse or remission, aggravating and relieving factors, diurnal variation
- History of jaundice, sore throat, diabetes, neck swelling (lymphoma)
- Past history of infections (malaria, leprosy) collagen vascular disorder (SLE), skin rashes
- Drug history and history of alcoholism

**General Physical Examination**

- General appearance – moon facies or puffiness of face, periorbital oedema xanthelasma
- Nutritional status
- Look for jaundice, anaemia, cyanosis
- Neck veins for JVP
- Lymph nodes
- Pulse and BP
- Skin for alopecia, rash, xanthomas
- Feet for pitting oedema
- External genitalia for oedema and hydrocoele.



**Fig. 1.18:** A patient with puffiness of face and oedema feet. There was ascites and scrotal oedema. There was no anaemia, jaundice or cyanosis. Blood pressure was normal. CVS examination was normal

**Systemic Examination**

1. Abdomen –distended, presence of ascites, oedema of abdominal wall, shiny skin, nontender renal angle, scrotal (or vulval) oedema, presence of hydrocoele
2. Respiratory system. Thoraco-abdominal respiration, oedema chest wall and legs, pleural effusions. Sometimes evidence of infection
3. CVS examination- non contributory.

**Clinical Presentations**

- The patients usually children, adolescents or adults present with puffiness of eyelids or periorbital oedema especially in the morning on awakening followed by oedema face and feet (Fig. 1.18).
- Patients with progressive disease present with ascites and generalised anasarca.
- Patients may present with complications, e.g. pulmonary infection, pleural effusion, thromboembolism, renal vein thrombosis, protein malnutrition and microcytic hypochromic anaemia.
- Patients may present with symptoms and signs of underlying disorder, i.e. infections (malaria, leprosy, syphilis, streptococcal sore throat), collagen vascular disorders, lymphomas, diabetes mellitus and toxæmia of pregnancy or hypertension.

**213. How do you define nephrotic syndrome?**

**Ans.** Nephrotic syndrome is defined as a heterogeneous clinical complex comprising of following features;

1. Massive proteinuria >3.5 g/day or protein/creatinine ratio of >400 mg/mmol
2. Hypoalbuminaemia/ hypoproteinaemia
3. Pitting pedal oedema
4. Hyperlipidaemia and lipiduria
5. Hypercoagulopathy.

**214. What are its causes?**

**Ans.** A wide variety of disease processes including immunological disorders, toxic injuries, metabolic abnormalities, biochemical defects and vascular disorders involving the glomeruli can lead to it (Table 1.61).

**Table 1.61:** Common causes of nephrotic syndrome

<b>1. Primary glomerular diseases</b>
a. Minimal change disease
b. Mesangioproliferative glomerulonephritis
c. Membranous glomerulonephritis
d. Membranoproliferative glomerulonephritis (crescents formation)
e. Focal glomerulosclerosis
<b>2. Secondary to other diseases</b>
<b>A. Infections</b>
a. Post-streptococcal glomerulonephritis
b. Post-streptococcal endocarditis
c. Secondary syphilis
d. Malaria (vivax and malariae infection)
e. Lepromatous leprosy
<b>B. Drugs and toxins</b>
Gold, mercury, penicillamine, captopril, antitoxins, antivenoms and contrast media
<b>C. Neoplasm</b>
a. Wilms' tumour in children
b. Hodgkin and non-Hodgkins lymphoma
c. Leukaemia
<b>D. Systemic disorders</b>
a. Systemic lupus erythematosus (SLE)
b. Goodpasture's syndrome
c. Vasculitis, e.g. polyarteritis nodosa
d. Amyloidosis
e. Diabetes mellitus
<b>E. Heredo-Familial</b>
a. Congenital nephrotic syndrome
b. Alport's syndrome
<b>F. Miscellaneous</b>
a. Toxaemia of pregnancy
b. Renovascular hypertension

**215. What is the clinical diagnosis of the patient in picture?**

**Ans.** Presence of morning puffiness of face followed by oedema feet during day time with ascites without hypertension in a young patient suggests the possibility of Nephrotic syndrome.

**216. What is its differential diagnosis?**

**Ans.** The differential diagnosis of nephrotic syndrome lies within the causes of ascites with anasarca (read differential diagnosis of ascites).

**217. What is its etiopathogenesis?**

**Ans.** Massive proteinuria >3.5 g/day is an essential criteria for the diagnosis. Other components are its consequences as described in Table 1.62.

**Table 1.62:** Pathogenesis of components of nephrotic syndrome

Components	Pathogenesis
Proteinuria	Altered permeability of GBM and the podocytes and their slit diaphragms
Hypoalbuminaemia	Increased urinary protein loss not compensated by increased hepatic synthesis of albumin
Oedema	Decreased oncotic pressure and stimulation of renin-angiotensin system resulting in salt and H <sub>2</sub> O retention.
Hyperlipidaemia and lipiduria	Increased hepatic lipoprotein synthesis triggered by reduced oncotic pressure
Hypercoagulability	<ul style="list-style-type: none"> <li>• Increased urinary loss of antithrombin III</li> <li>• Altered levels and/or activity of protein C and S</li> <li>• Hyperfibrinogenaemia</li> <li>• Impaired fibrinolysis</li> <li>• Increased platelet aggregation.</li> </ul>

**218. How will you investigate such a patient?**

**Ans.** Investigations of nephrotic patient are as follows:

1. *Urine examination* reveals proteinuria and casts (fatty casts). Haematuria is uncommon.
2. *24 hours urine* shows excretion of albumin or proteins >3.5 g or protein/creatinine ratio >400 mg/mmol. In early stages of the disease or in patients receiving treatment, the proteinuria may be less.
3. *Serum lipids.* Low density lipoproteins and cholesterol are increased in majority of the patients. Hyperlipidaemia is an integral component of the syndrome.

4. *Serum proteins or albumin.* Total serum proteins may be normal or low. Serum albumin is usually low <3 g/dl, also forms an important diagnostic criteria.
5. *Other renal function tests,* e.g. blood urea, creatinine, creatinine clearance and electrolytes are normal in uncomplicated cases, become abnormal if renal failure sets in.
6. *Chest X-ray* may show hydrothorax.
7. *Ultrasound of abdomen.* It may show normal, small or large kidneys depending on the cause. Amyloid and diabetic kidneys are large; while kidneys in glomerulonephritis are small.
8. *Renal biopsy.* It is done in adult nephrotic syndrome to show the nature of underlying disease, to predict the prognosis and response to treatment.

Renal biopsy is not required in majority of children with nephrotic syndrome as most of them belong to minimal change disease and respond to steroids.

### 219. What is selective and nonselective proteinuria?

**Ans.** *Selective proteinuria* means filtration of low molecular weight proteins especially the albumin through the glomeruli. It is seen in minimal change glomerulonephritis and early phase of other glomerulonephritis. These cases respond well to steroids.

*Nonselective proteinuria* means filtration of albumin along with high molecular weight proteins, e.g. globulins, antithrombin III, transferrin, immunoglobulins, thyroxine-binding globulins, calciferol-binding globulin, etc. This occurs in advanced glomerular disease and does not respond to steroids. It is a bad prognostic sign. The loss of these proteins constitute the clinical spectrum of the nephrotic syndrome in adults.

### 220. What are the differences between glomerular proteinuria and tubular proteinuria?

**Ans.** Following are the differences:

**Glomerular proteinuria.** The damage to the glomeruli allows filtration of larger molecular weight proteins especially the albumin. The presence of albumin in the urine is sure sign of glomerular abnormality. The proteinuria in glomerular disease is >1 g/day. The severity of proteinuria is a marker for an increased risk of progressive loss of renal function. The glomerular proteinuria is associated with cellular casts (RBCs, WBCs) which are dysmorphic, i.e. get distorted as they pass through the glomerulus.

**Tubular proteinuria** is secretion of Tamm-Horsfall proteins or excretion of low molecular weight proteins especially retinol-binding proteins,  $\beta$ -macroglobin. The proteinuria is <1 g/day occurs in tubulo-interstitial diseases. Tubulointerstitial diseases are not the cause of either nephritic or nephrotic syndrome. The casts in tubulointestinal diseases are epithelial or granular.

### 221. What are characteristics of minimal change disease (MCD) or lipoid nephrosis, nil disease or foot process disease?

**Ans.** The characteristic features are:

- i. Most common cause of nephrotic syndrome in children (70-80%) and more common in males than females.
- ii. It is named so because light microscopy of renal biopsy specimen does not reveal any abnormality of glomeruli. Electron microscopy reveals effacement of the foot processes of epithelial cells
- iii. Proteinuria is highly selective.
- iv. Haematuria is uncommon.
- v. Spontaneous relapses and remissions are common.
- vi. Majority of the patients respond promptly to steroids. The disease may disappear after steroid therapy.
- vii. Progression to acute renal failure is rare.
- viii. Prognosis is good.

### 222. What are characteristics of membranous glomerulonephritis?

**Ans.** The characteristic features are as follows:

- i. It is a leading cause of nephrotic syndrome in adults (30-40%) but is a rare cause in children.
- ii. It has peak incidence between the ages of 30 and 50 years, more common in males.
- iii. It is named so because the light microscopy of renal biopsy specimen shows diffuse thickening of glomerular basement membrane (GBM) which is most apparent on PAS staining
- iv. Proteinuria is nonselective
- v. Haematuria is common (50%)
- vi. Spontaneous remissions may occur in only 30-40% patients
- vii. Renal vein thrombosis is a common complication.
- viii. Response to steroids therapy is inconsistent, it may reduce proteinuria but does not induce remission.
- ix. 10-20% cases progress to end-stage renal disease (ESRD) requiring transplantation of kidney.



**223. What are complications of nephrotic syndrome?**

**Ans.** Common complications are as follows:

**1. Vascular**

- Accelerated atherogenesis due to hyperlipidaemia leading to accelerated hypertension and early coronary artery disease.
- Peripheral arterial or venous thrombosis, renal vein thrombosis and pulmonary embolism due to hypercoagulable state.

**2. Metabolic**

- Protein malnutrition
- Iron-resistant microcytic hypochromic anaemia
- Hypocalcaemia and secondary hyperparathyroidism.

**3. Infections**

- Pneumococcal and staphylococcal infections (respiratory and peritonitis) due to depressed immunity (low levels of IgG).

**4. Chronic renal failure****224. What are causes of hypertension in nephrotic syndrome?**

**Ans.** Hypertension is not a feature of nephrotic syndrome, but may be seen in diseases that cause nephrotic syndrome such as;

- Diabetic nephropathy
- SLE and polyarteritis nodosa
- Nephrotic syndrome complicated by CRF
- Focal glomerulosclerosis is commonly associated with hypertension.

**225. What is indication of renal biopsy in nephrotic syndrome?**

**Ans.** The renal biopsy is done for following reasons:

- To confirm the diagnosis
- To know the underlying pathological lesion
- To plan future treatment
- To predict the prognosis and response to treatment.

**226. What is the common pathological lesion in diabetic nephropathy?**

**Ans.** Kimmelstiel-Wilson syndrome (diabetic nodular glomerulosclerosis) is the common pathological lesion.

- It occurs commonly in type I diabetes than type 2 diabetes
- Usually develops as a long-term microvascular complication of diabetes (duration of diabetes >10 years)
- Common presentation is moderate to massive proteinuria. Hypertension may develop later on.
- With the onset of this lesion, the requirement of insulin falls due to excretion of insulin antibodies in urine.
- Progresses to end-stage renal disease (ESRD) over a period of few years.
- The characteristic histological lesion is nodular glomerulosclerosis.

**227. How does nephrotic syndrome differ from nephritic syndrome?**

**Ans.** The differences are tabulated (Table 1.63)

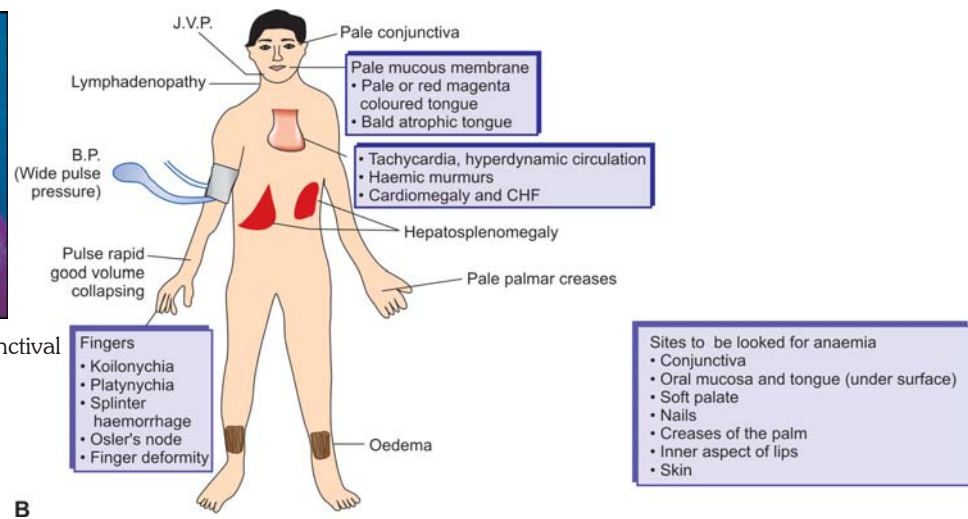
**Table 1.63:** Differences between nephrotic and nephritic syndrome

Feature	Nephrotic syndrome	Nephritic syndrome
Onset	Slow, insidious chronic disorder	Sudden, acute renal disorder
Proteinuria	Massive > 3.5 g/d	Moderate 1-2 g/d
Hyperlipidaemia and lipiduria with faulty casts	Present	Absent
Hypertension	Not a feature	An important feature
Volume of urine passed in 24 hr	Normal	Oliguria
Haematuria	Not common	A common and integral component of syndrome
Acute renal failure	Uncommon	Common
Relapse and remission	Common	Uncommon
Course	Chronic progressive disorder	70-80% cases recover completely while others pass on to RPGN

## CASE 19: ANAEMIA



The patient has pale tongue, conjunctival along with puffiness of face



**Figs 1.19A and B:** A. A patient with severe anaemia. B. Clinical features of anaemia

A 19 years female (Fig. 1.19A) presented with pallor, fatigue, malaise, weakness and breathlessness on exertion. There was no history of fever, loose motion, blood loss, any surgery. No history of drug intake. She has generalised pallor with slight puffiness of face.

#### Points to be noted in History

- Symptoms and their analysis
- History of fever, blood loss, drug intake loose motion, jaundice, dysphagia, vomiting
- Menstrual history, history of recent delivery and blood loss if any
- History of piles or repeated haematemesis
- Nutritional history
- Past history of tuberculosis, bleeding, any surgery, trauma, repeated abortions/deliveries
- Personal history, e.g. alcoholism
- Family history of jaundice.

#### General Physical Signs

- Facial appearance or look
- Puffiness of face or periorbital oedema
- Look for anaemia at different sites, koilonychia, platynychia, bleeding from gums or nose
- Neck examination for JVP, lymphnodes and thyroid

#### Clinical Presentations

- Patients with mild anaemia are asymptomatic. Anaemia is discovered on routine haemoglobin estimation done for some other purposes. On symptomatic enquiry, they may admit history of occasional exertional dyspnoea, palpitations and fatigue.
- Patients with severe anaemia usually complain of weakness, weight loss, dyspnoea, palpitation, throbbing headache, dizziness, tinnitus and menstrual irregularity in females, tingling in extremities and GI symptoms (nausea, anorexia).
- Anaemia may be a presenting feature of certain chronic disorders, e.g. malabsorption, chronic renal failure, chronic blood loss (haematemesis, malaena, menorrhagia) or malignant disorders.

*Note* Anaemia is a sign not a complete diagnosis, hence, cause of anaemia must be mentioned in the diagnosis e.g. malabsorption with anaemia, CRF with anaemia etc.

#### Systemic Examinations

##### I. Examination of CVS

###### Inspection

- Look for apex beat, e.g. location, type
- Any chest deformity
- Chest movements

###### Palpation

- Trachea—Note any deviation
- Apex beat—confirm the findings of inspection
- Chest movements and expansion

###### Percussion

- Heart borders, cardiac and liver dullness
- Lung resonance

###### Auscultation

- Heart, e.g. sounds, murmurs, if any murmur, note its various characteristics
- Lung sounds, e.g. breath sounds, crackles and rales

##### II. Examination of abdomen

###### Inspection

- Contour, shape of umbilicus, hernial sites, any swelling or mass or distension

###### Palpation

- Palpate for any mass

- Pulse, BP, temp, respiration
- Skin for any bleeding spots or rash
- Oedema feet
- Look for deficiency signs of hypoproteinaemia, e.g. flabby muscles, wasting, thin skin.

- Palpate for liver, spleen and kidneys
- Elicit any tenderness

*Percussion*

- Percussion note. Note over the mass if present. Define upper border of the liver

*Auscultation*

Hear for sound, bruit or rub

**III. Examination of CNS**

- Look for signs of neuropathy

**IV. Endocrine system**

- Look for signs of hyper or hypothyroidism.

**228. What is the clinical diagnosis of the patient in picture?**

**Ans.** The young patient presented with exertional breathlessness, fatigue and malaise. She was found to have generalised pallor and paleness of mucous membrane. The clinical diagnosis is anaemia the cause of which is nutritional.

**229. How do you define anaemia?**

**Ans.** A hemoglobin level  $\leq 11.0\%$  g in an adult female and  $< 12.0\%$  g in an adult male is taken as anaemia.

**230. What are symptoms and signs of anaemia?**

**Ans.** For symptoms – read clinical presentations. For sign – see Figure 1.19B.

**231. What are the causes of anaemia?**

**Ans.** The common clinical causes of anaemia in India are:

- Nutritional, e.g. deficient intake of iron, folate and protein in diet
- Hookworm infestation
- Chronic blood loss, e.g. piles, haematemesis, menorrhagia, malaena etc.
- Chronic diarrhoea and malabsorption.
- Pregnancy associated anaemia
- Hypoproteinaemia, e.g. nephrotic syndrome, cirrhosis liver
- Haemolytic anaemia, e.g. malarial parasite or drug-induced in G6PD deficiency.
- Anaemia of chronic infection, e.g. tuberculosis, SLE, rheumatoid arthritis.
- Anaemia associated with malignancies, e.g. leukaemia, lymphoma, carcinoma stomach, colon etc.
- Hereditary anaemia.

**232. What are common causes of iron deficiency anaemia (microcytic hypochromic)?**

**Ans.** Common causes are as follows:

1. Nutritional deficiency, e.g. inadequate iron intake
2. Increased demands, e.g. pregnancy and lactation
3. Blood loss
  - GI loss, e.g. bleeding peptic ulcer, piles, haematemesis, hookworm disease
  - Uterine, e.g. menorrhagia, repeated abortions, dysfunctional uterine bleeding
  - Renal – haematuria
  - Nose – epistaxis
  - Lung – haemoptysis
4. Malabsorption due to any cause.

**233. What are clinical signs of iron deficiency anaemia?**

**Ans.** Clinical signs are:

- Pallor
- Glossitis, angular stomatitis, cheilosis
- Koilonychia
- Dysphagia (Plummer – Vinson syndrome)
- Mild splenomegaly
- History of *pica* (eating of strange items, e.g. coal, earth).

**234. What is sideroblastic anaemia (nonutilization of iron)? What are its causes?**

**Ans.** A red cell containing iron is called *siderocyte*. A developing erythroblast with one or two iron granules is called *sideroblast*. Iron granules free in cytoplasm of RBCs are normal, but when they form a ring round the nucleus in red cells, then they are considered abnormal and called *ring sideroblasts*. The anaemia in which ring sideroblasts

are present is called *sideroblastic anaemia*. It is due to nonutilisation of the iron in the bone marrow resulting in accumulation of iron as granules in developing red cells. Sideroblastic anaemia may be primary (hereditary or congenital) or secondary (acquired). The causes are:

1. *Hereditary (congenital)*
2. *Acquired*
  - Inflammatory conditions
  - Malignancies
  - Megaloblastic anaemias
  - Hypothyroidism
  - Drug induced
  - Lead poisoning
  - Pyridoxine deficiency.

### 235. What are causes of megaloblastic anaemia?

**Ans.** It occurs due either to folate or Vit. B<sub>12</sub> deficiency or both. The causes are:

1. Nutritional, e.g. inadequate intake, alcoholism.
2. Increased demands of folic acid, e.g. pregnancy, lactation.
3. Following haemolysis
4. Malabsorption syndrome;
  - Ileal disease
  - Gastrectomy
  - Blind – loop syndrome
5. *Drug induced*, e.g. anticonvulsants, methotrexate, oral contraceptive, pyrimethamine.
6. *Parasitic infestation*, e.g. *Diphyllobothrium latum*.

### 236. What are causes of haemolytic anaemia?

**Ans.** (Read haemolytic jaundice).

### 237. What are causes of aplastic anaemia?

**Ans.** Followings are the causes:

1. **Primary** – red cell aplasia.
2. **Secondary**
  - i. *Drugs*
    - Dose related, e.g. methotrexate, busulfan, nitrosourea
    - Idiosyncratic, e.g. chloramphenicol, sulpha drugs, phenylbutazone, gold salts.
  - ii. *Toxic chemicals*, e.g. insecticides, arsenicals, benzene derivatives
  - iii. *Infections*, e.g. viral hepatitis, AIDS, other viral infections

- iv. *Miscellaneous*, e.g. irradiation, pregnancy, paroxysmal nocturnal haemoglobinuria.

### 238. What are causes of reticulocytosis and reticulopenia?

**Ans.** *Reticulocyte* is a young red cell with basophilic cytoplasm (polychromasia). It matures into an adult RBC within 3 days. The normal reticulocyte count is 0.5-2% in adults and 2-6% in infants. An absolute increase in reticulocyte count is called *reticulocytosis*. The causes are;

- Haemolytic anaemia
- Accelerated erythropoiesis
- Polycythemia rubra vera

*Reticulocytopenia* means low reticulocyte count ( $\leq 0.5\%$ ) is seen in aplastic anaemia and *megaloblastic anaemia*.

### 239. Name the chronic systemic diseases associated with anaemia

**Ans.** Following are the systemic diseases:

- Chronic infections, e.g. tuberculosis, SABA, osteomyelitis, lung suppuration
- Collagen vascular disorders, e.g. SLE
- Rheumatoid arthritis
- Malignancy anywhere in the body
- Chronic renal failure
- Endocrinal disorders, e.g. Addison's disease, myxedema, thyrotoxicosis, panhypopituitarism
- Cirrhosis of the liver especially alcoholic.

### 240. What is morphological classification of anaemia?

**Ans.** Morphological classification refers to average size and haemoglobin concentration of RBCs.

1. *Microcytic hypochromic* (reduced MCV, MCH and MCHC )
  - Iron deficiency anaemia
  - Sideroblastic anaemia
  - Thalassaemia
  - Anaemia of chronic infection
2. *Normocytic normochromic* (MCV, MCH and MCHC normal)
  - Haemolytic anaemia
  - Aplastic anaemia

3. Macrocytic (MCV is high. MCH and MCHC relative low)
  - Folate and Vit. B<sub>12</sub> deficiency (read the causes of megaloblastic anaemia)
4. Dimorphic anaemia (microcytic as well as macrocytic)
  - Nutritional deficiency
  - Pregnancy
  - Malabsorption syndrome
  - Hookworm infestation.

**241. What are diagnostic clues to hookworm infestation?**

**Ans.** The clues are:

- Occupation (e.g. workers in tea – garden, farmers, coal-miners)
- History of walking bare-footed
- Presence of ground itch in interdigital spaces
- Pain abdomen (epigastrium simulating peptic ulcer)
- History of pica
- Diarrhoea or steatorrhoea
- Iron deficiency or dimorphic anaemia
- Prevalence of hookworm disease in that area.

**242. How will you investigate a patient with anaemia?**

**Ans.** Investigations are done to confirm anaemia and to find out the cause of anaemia:

*Test to Confirm Anaemia*

- Haemoglobin and red cell count
- Peripheral blood film for type of anaemia and to find out any abnormality of the shape of RBCs and presence of malarial parasite or any other abnormal cells. Reticulocytosis indicates accelerated erythropoiesis.
- Bone marrow examination. It provides assessment of cellularity, details of developing RBCs, assessment of iron store, presence of marrow infiltration by parasites, fungi and secondary carcinoma.

*Specific Tests*

*For iron deficiency anaemia*

- Serum iron is low
- Iron binding capacity is raised
- Serum ferritin low.

*For megaloblastic anaemia*

- Plasma LDH markedly elevated
- Serum iron elevated
- Serum ferritin elevated
- Serum bilirubin – unconjugated hyperbilirubinaemia
- Antiparietal cell antibodies and an abnormal Vit. B<sub>12</sub> absorption, studies (Schilling test) may be observed in Vit B<sub>12</sub> deficiency anaemia or pernicious anaemia.
- Serum folate levels/ Red cell folate levels.

*For Haemolytic anaemias*

- PBF for morphology of the RBCs (spherocytes, ovalocytes, elliptocytes, sickle cells) and for malarial parasite
- Haemoglobin electrophoresis for thalassaemia (HbF > 2%)
- Coombs' test (direct and indirect)—may be abnormal
- Osmotic fragility test may be positive
- Serum bilirubin shows unconjugated hyperbilirubinaemia
- Red cell survival studies may reveal decreased survival
- Sickling test positive in sickle cell anaemia.

**243. What are causes of refractory anaemia?**

**Ans.** The anaemia that does not respond to appropriate treatment given for optimal period is called *refractory anaemia*. The causes are:

- Aplastic anaemia
- Thalassaemia
- Sideroblastic anaemia (pyridoxine-responsive)
- Refractory anaemia due to myelodysplastic syndrome.
- Anaemia due to leukaemia, e.g. erythroleukaemia or aleukaemic leukaemia,



**CASE 20: LEUKEMIA**

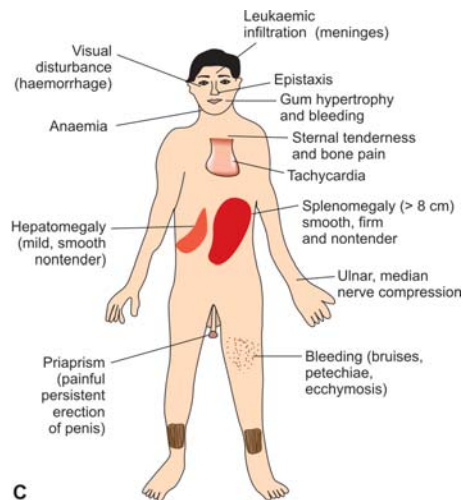
A patient (Fig. 1.20A) presented with fever, dyspnoea and bleeding from the nose. There was history of a big mass in the left hypochondrium with dragging pain. Another patient (Fig. 1.20B) presenting with bleeding from the gums, excoriation of mouth, fever, breathlessness and pallor. There was also history of mass abdomen and pain abdomen.

**Points to be Noted in History**

- Onset and progression of symptoms
- History of fever, sore throat, ulceration in the mouth
- History of bleeding from any site, e.g. gum, nose, urine, sputum, skin
- History of weakness of any part of the body, convulsions
- History of visual impairment or loss
- History of breathlessness, fatigue or pain abdomen.

**General Physical Examination**

- **Face:** expression, puffiness
- **Oral cavity,** e.g. gum bleeding, anaemia or excoriation or aphthous ulceration
- **Neck examination** for JVP, lymphadenopathy, thyroid enlargement
- **Pulse, BP, temperature and respiration**
- **Hands** for koilonychia or platynychia, clubbing, sublingual haematoma or bleeding
- **Skin** for bleeding spots or ecchymotic patches
- Elicit **sternal tenderness**
- **Oedema feet**



**Figs 1.20A to C: Chronic myeloid leukaemia.** A. Patient presented with epistaxis. B. Patient presented with gum bleeding. C. Clinical manifestation of CML (diagram)

**Clinical Presentations**

- Patients with acute leukaemia usually children or adolescents present with acute onset of symptoms and signs of bone marrow failure, i.e. anaemia (pallor lethargy, dyspnoea, palpitations,

**Systemic Examination****Examination of abdomen***Inspection*

- A mass in the left Rypo-chondrium. Describe all its characteristics
- Shape and position of the umbilicus may be normal or disorted by the mass if it is huge
- Hernial sites normal.

*Palpation*

- A palpable mass in left and right hypochondrium. Described its characteristics
- Any tenderness of abdomen.

*Percussion*

- Percuss over the mass. There will be dullness over splenic and liver mass
- Normal abdominal resonance
- Define the upper border of liver to confirm liver enlargement

*Auscultation*

- Auscultate the bowel sounds
- Auscultate over the mass for any bruit, rub etc.

**Other Systems***CVS Examination*

- Look for anaemia
- Auscultate for sounds, murmurs or rubs
- Looks for signs of CHF

*Nervous System*

- Look for entrapment neuropathy, e.g. carpal tunnel syndrome or peripheral neuropathy.

- etc.), thrombocytopenia (bleeding from gums, epistaxis, petechiae and spontaneous bruising) and neutropenia (infections leading to fever, excoriation of mouth and respiratory infection). They may also present with hepatosplenomegaly and/ or lymphadenopathy.
- Patients with chronic leukaemia usually middle aged or old persons present with insidious onset of symptoms of anaemia, bone pain, infections (fever) and bleeding tendencies. These cases especially with chronic myeloid leukaemia present with mass abdomen while that of chronic lymphoid leukaemia with lymphadenopathy and splenomegaly. A significant number of cases are discovered incidentally.

Hepatosplenomegaly with anaemia is classic feature of CML. A mass abdomen with dragging pain is a presenting feature

**244. What is the clinical diagnosis of the patients in picture?**

**Ans.** Both the patients are young and presented with bleeding from nose (A) and gums (B) with a mass in left abdomen (both patients), the diagnosis of chronic myeloid leukaemia is most likely.

**245. How do you define leukaemia? What is subleukemic or aleukaemia leukaemia?**

**Ans.** The leukaemias are a group of white cell disorders characterised by malignant transformation of blood white cells primarily in the bone marrow resulting in increased number of primitive white cells (blasts cells) in the bone marrow which ultimately spill into peripheral blood raising the total leucocyte count in peripheral blood.

*Subleukaemic or aleukaemic leukaemia* is defined as the presence of immature cells in the bone marrow with little or no spilling into peripheral blood, hence, the WBC count is not high; may be normal or even reduced. The diagnosis is confirmed on bone marrow examination.

**246. What is difference between acute and chronic leukaemia?**

**Ans.** Depending on the clinical behaviour of leukaemia, it has been classified into acute and chronic. In **acute**

leukaemia, the history is short and life expectancy without treatment is short while in **chronic** leukaemias, the patient is unwell for months and survives for years. The difference between acute and chronic leukaemia are summarised in Table 1.64.

**Table 1.64:** Differentiation between acute and chronic leukaemias

Acute	Chronic
Common in children and adolescents	Common in adults and old age
Acute onset	Slow insidious onset
Presentation is bone marrow failure i.e. anaemia, thrombocytopenia and leucopenia with their systemic effects	Presentation is extramedullary hematopoiesis, e.g. hepatosplenomegaly
Cell count varies in thousands, usually does not cross a lac	Cell count varies in lacs
Predominant cell type is blast cells	Predominant cell type is cytic cells (myelocytic, premyelocytic, metamyelocytic)
Blast cells usually exceed 30% in the marrow	Blast cells are usually less than 10%
Prognosis is bad, usually months to a year	Prognosis is good usually few years

**247. How do you classify leukaemias?**

**Ans.** The leukaemia on the basis of cell types are classified into *myeloid* and *lymphoid* and on the basis of natural history into acute and chronic as described above. The subclassification of leukemia is depicted in Table 1.65.

**Table 1.65:** Subclassification of leukaemia

<p><b>1. Acute lymphoblastic</b></p> <ul style="list-style-type: none"> <li>• Common type (Pre B)</li> <li>• T cell</li> <li>• B cell</li> <li>• Undifferentiated</li> </ul> <p><b>2. Acute myeloid (FAB* classification)</b></p> <p>Mo= Undifferentiated M1= Minimal differentiation M2= Differentiated M3= Promyelocytic M4= Myelomonocytic M5= Monocytic M6= Erythrocytic M7= Megakaryocytic</p> <p><b>3. Chronic lymphocytic/lymphoid</b></p> <ul style="list-style-type: none"> <li>• B cell – common</li> <li>• T cell – rare</li> </ul> <p><b>4. Chronic myeloid</b></p> <ul style="list-style-type: none"> <li>• Ph' positive</li> <li>• Ph' negative, BCR – abl positive</li> <li>• Ph' negative</li> <li>• Eosinophilic leukaemia</li> </ul>	<p>FAB = French, American, British Ph' = Philadelphia chromosome BCR = Break point cluster region abl; Abelson oncogene</p>
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**248. What are symptoms and signs of leukaemia?**

**Ans.** Clinical symptoms are:

**1. Symptoms due to anaemia**

- Weakness
- Dyspnoea
- Pallor
- Tachycardia

**2. Symptoms due to hypermetabolism**

- Weight loss
- Lassitude
- Anorexia
- Night sweats

**3. Symptoms due to hyperplasia of bone marrow or infiltration of marrow by leukaemic cells**

- Bone pain
- Sternal or iliac tenderness

**4. Symptoms due to infection**

- Fever
- Perspiration

**5. Bleeding tendencies**

- Easy bruising, ecchymosis
- Epistaxis
- Menorrhagia
- Hematomas

**6. Symptoms of hyperuricaemia produced by drug treatment**

- Asymptomatic
- Uric acid stones
- Precipitation of an attack of gout
- Uric acid nephropathy

**249. How will you arrive at the diagnosis of CML? What is its differential diagnosis?**

**Ans.** CML is diagnosed on the clinical findings and confirmed on investigations.

- *Clinical findings in CML*
- Adult patient
- Gradual onset of dragging pain and mass in the left hypochondrium
- Progressive anaemia; anorexia, abdominal fullness, marked weight loss
- Moderate hepatomegaly with huge splenomegaly (> 8 cm below the costal margin)
- Sternal tenderness

*Confirmation of CML*

- Peripheral blood and bone marrow examination
- Ph' chromosome, if present, clinches the diagnosis
- Low leucocyte alkaline phosphatase score
- RNA analysis for presence of BCR-abl oncogene

*Differential Diagnosis*

Differential diagnosis of CML is actually the differential diagnosis of hepatosplenomegaly (read hepatosplenomegaly and splenomegaly).

**250. What are causes of bleeding gums?**

**Ans.** • Leukaemias, e.g. acute (myelomonocytic common) and chronic (CML)

- Bleeding disorders, e.g. thrombocytopenia scurvy
- Dilantin toxicity (hypertrophy cum gum bleeding)
- Gingival disorders
- Local trauma

**251. What are causes of sternal tenderness?**

**Ans.** Sternal tenderness is usually due to expansion of the bone marrow due to its proliferation, hence, can be present in all those conditions which cause bone marrow proliferation, i.e.

- Acute leukaemia (AML and ALL)
- CML
- Severe anaemia especially acute haemolytic anaemia or crisis
- Multiple myeloma
- Following sternal puncture. This is easily diagnosed by the presence of either sternal puncture mark or attached cotton seal or benzene stain over sternum.

**252. What are complications of CML?**

**Ans.** Common complications of CML are as follows:

- Blastic crisis or blastic transformation of CML
- Haemorrhage or bleeding
- Recurrent infections (respiratory infection common)
- Hyperuricaemia (due to disease as well as treatment)
- Leukaemic infiltration in cranial nerves (compression neuropathy), pleura (pleural effusion), bones (paraplegia)
- Priapism – persistent painful erection of penis
- Infarction or rupture of the spleen. Presence of splenic

rub indicates infarction; while tender spleen can occur both in infarction and rupture.

Conversion of CML to acute leukemia indicates blastic crisis.

**253. What is blastic crisis?**

**Ans.** It refers to transformation of chronic stable phase of chronic leukaemia into acute unstable phase characterised by progressive anaemia, onset of severe bleeding (e.g. petechiae, bruises, epistaxis, GI bleed) and on examination one would find;

- Sternal tenderness
- Appearance of lymphadenopathy (due to transformation to ALL).

The diagnosis is confirmed by peripheral blood examination which shows >30% blast cells (usually in CML, blast cells are <10%).

**N.B.:** Blastic crisis in CML is seen in patients with long duration of disease being treated with myelosuppressive drugs.

**254. What are differences between acute myeloid and acute lymphoid leukaemia?**

**Ans.** The ALL is common in children while AML is common in adults. The contrasting features of two types of leukaemia are summarised in Table 1.66.

**Table 1.66:** Two common types of acute leukaemia—similarities and dissimilarities

Feature	AML	ALL
Age	Adults (15-40 years)	Children (<15 years)
Incidence	Constitutes 20% of childhood leukaemia	Constitute 80% of childhood leukaemia
Symptoms	Fever, tiredness, bleeding manifestations, mouth ulceration and recurrent infections	Same as AML. Bone pain and tenderness common
Physical findings	Hepatosplenomegaly (+) Lymphadenopathy (+) Gum hypertrophy (+) Bone tenderness (+) Chloroma (common) i.e. localised tumour masses in orbit, skin and other tissue Anaemia (++) Leukaemic meningitis (uncommon) Sternal tenderness (++)	Hepatosplenomegaly (+++) Lymphadenopathy (++) Gum hypertrophy (++) Bone tenderness (++) Chloroma – rare
Laboratory findings	Low to high WBC count with predominant myeloblasts (>30%)	Low to high WBC count with predominant lymphoblasts
Cytochemical	Myeloperoxidase positive	PAS positive
Stain	Sudan black positive	—
Remissions	Remission rate is low, duration of remission short	Remission rate high and duration of remission prolonged

Signs used (+) means present (++) to (+++) means a marked feature

**Table 1.67:** Similarities and dissimilarities between CML and CLL

Feature	CML	CLL
Age	Peak age 55 years	Peak age 65 years
Onset	Insidious	Very insidious
Symptoms and signs	Hepatosplenomegaly marked Anaemia early Lymphadenopathy uncommon Sternal tenderness present Blast crisis (common)	Hepatosplenomegaly mild Anaemia develops late Lymphadenopathy is common presentation Sternal tenderness absent Blast crisis (uncommon)
Laboratory findings	Very high WBC count with predominant myelocytes and metamyelocytes Philadelphia chromosome positive	WBC count high, predominant cells are lymphocytes Philadelphia chromosome negative
Response to treatment	Good	Excellent
Prognosis	Good	Excellent

**255. What are similarities between CML and CLL? How they differ from each other?**

**Ans.** Table 1.67 differentiates between CML and CLL.

**256. What is significance of Philadelphia Chromosome?**

**Ans.** The significances are:

- The philadelphia chromosome (Ph') results from reciprocal translocation between the parts of long arms of chromosomes 9 and 22.
- Found in 90% cases of CML. Rest 10% are philadelphia chromosome negative. It is considered as diagnostic tool for CML.
- Ph'-chromosome positive cases have better prognosis than Ph'- chromosome negative cases.
- It is found in myeloid and erythroid series of blood cells in bone marrow. It is never seen in lymphocytes.
- It can differentiate AML from blastic crisis in CML
- Philadelphia chromosome is positive throughout the course of the disease during treatment, however, philadelphia positive cells decrease with alpha-interferon and Initab mesylate (STI 571) therapy.

**257. How will you investigate a case with CML?**

**Ans.** Investigations are as follows:

1. *Blood examination*
  - Haemoglobin and RBC count. They are low

- WBC count high ( $1-5 \text{ lac/mm}^3$ ). Differential count shows 20-30% myelocytes, 20-25% metamyelocytes, 2-3% promyelocytes and rest are polymorphs. Myeloblasts ( $< 10\%$ ) may be seen. There may be increase in basophils and eosinophils in early disease.
- Platelet count – normal to increased in early stages but decreased in late stages.

2. *Bone marrow examination.* It is not must for diagnosis as presence of immature cells ( $>30\%$ ) in the peripheral blood are sufficient for diagnosis. It shows increased myelocyte series of cells with increased myeloid and erythroid ratio (20:1). Bone marrow is hypercellular. Myeloblasts  $>30\%$  in the bone marrow in CML indicates blastic crisis.
3. Chromosomal study for philadelphia chromosome. It is positive in 90% cases
4. RNA analysis for BCR-abl oncogene
5. Leucocyte alkaline phosphatase score is diminished
6. Other tests
  - High uric acid and LDH level
  - High serum Vit. B<sub>12</sub> level

**258. What is busulphan lung?**

**Ans.** Interstitial lung fibrosis seen during therapy with busulphan is called *busulphan lung*.



## CASE 21: LYMPHADENOPATHY

The patient 30 year male (Fig. 1.21) presented with multiple swelling in the neck with low grade fever, fatigue and malaise for the last 8 months.

### Points to be Noted in History

- Any history of swelling in the axilla or groin
- Any history of pain abdomen or mass abdomen (e.g. spleen and/or liver)
- Any history of fever, night sweats, fatigue, malaise and weight loss
- Any history of cough, dyspnoea or hoarseness of voice (for hilar lymphadenopathy)
- Any history of injury or infection of neck or extremity
- Past history of fever, tuberculosis, malignancy or injury/infection.

### General Physical Examination

- **Face** for puffiness or oedema
- **Mouth** for anaemia or evidence of infection  
Skin for evidence of bleeding or infection.
- **Neck.** Examine the lymph nodes and describe the number, consistency, tenderness, matting, adherence to underlying structures or overlying skin. Note the temperature over the mass. Look for JVP and thyroid. Examine axilla and inguinal region in addition to all other sites of lymph node. Examine the neck for preauricular, post-auricular, submental, etc (see Fig. 1.21B).
- Look for *engorgement of neck/chest veins, suffusion of the face and cyanosis* (e.g. superior mediastinal compression).
- Pulse, BP respiration and temperature
- Look for *anaemia, jaundice, oedema*, etc.



**Fig. 1.21:** A patient with cervical lymphadenopathy presented with mass in the neck which has irregular surface, is firm in consistency, adherent to overlying skin with a sinus and skin discolouration

### Clinical Presentations

1. **Asymptomatic.** Lymphadenopathy may be an incidental finding in patients being examined for various reasons.
2. **When symptomatic,** the symptoms may vary according to size, site and cause of involvement. They may present with:
  - Multiple swellings at one site or at different sites, e.g. neck, axillae and groins.
  - Mediastinal lymph node enlargement may present as superior mediastinal compression syndrome or superior vena caval obstruction syndrome
  - Intra-aortic abdominal lymph node enlargement produce pain abdomen and mass abdomen.
3. Patients may present with P.U.O. (fever), night sweats, weight loss or pain in the nodes.
4. Patients may present with the symptoms and signs of basic disease, e.g. leukaemia, lymphoma, acute infections etc. and lymphadenopathy is a part and parcel of the clinical spectrum.

### Systemic Examinations

- I. **Examination of abdomen**
  - Inspect the abdomen for any swelling or protuberance
  - Palpate the abdomen for liver, spleen or lymph node enlargement
  - Look for the presence of ascites.
- II. **Examination of respirator system**
  - Inspect the chest for any retraction or deformity
  - Palpate the trachea for any deviation
  - Look for any evidence of mediastinal shift due to lung collapse
  - Look for signs of superior mediastinal compression, e.g. periorbital oedema, chemosis, conjunctival suffusion, prominence of neck veins and veins over the chest, absent venous pulsation in the neck.
- III. **Examination of haematopoietic system**
  - Look for any evidence of purpuric or ecchymotic patches
  - Elicit sternal tenderness
  - Any evidence of infection
  - Ocular fundus examination.

**259. What the clinical diagnosis of the patient in picture?**

**Ans.** The presence of a lobulated irregular mass with irregular surface, form inconsistency, not mobile, fixed to the skin with formation of a sinus and skin pigmentation indicate a lymph node mass due to tuberculosis, e.g. tubercular lymphadenitis with sacrofuloderma.

**260. How do you define lymphadenopathy? What is meant by significant lymphadenopathy?**

**Ans.** Lymphadenopathy literally means enlargement of lymph nodes which may be significant or insignificant. *Significant lymphadenopathy* means enlargement that needs further evaluation. Lymph nodes enlargement  $\geq 1$  cm in size any where in the body is considered as significant except the groin where  $\geq 2$  cm size of the lymph node is considered significant. Insignificant enlargement means nonspecific, small lymph nodes usually  $<0.5$  cm in diameter, may be palpable due to past infection.

**261. What are the causes of lymphadenopathy?**

**Ans.** Localised or regional lymphadenopathy implies involvement of a single anatomical area. A generalised adenopathy has been defined as involvement of three or more noncontiguous lymph node areas. Many of the causes of lymphadenopathy (Table 1.68) can produce localised or generalised adenopathy, so this distinction is of limited utility in differential diagnosis.

**262. What are common causes of generalised lymphadenopathy?**

**Ans.** Nevertheless, generalised lymphadenopathy is frequently associated with nonmalignant disorders rather than malignant disorders. The common causes are:

- Tuberculosis
- Infectious mononucleosis
- Toxoplasmosis
- AIDS and other viral infections
- Collagen vascular disorders, e.g. SLE, mixed connective tissue disorders
- Leukaemias, e.g. acute and chronic lymphocytic leukaemias
- Lymphomas (Hodgkin's and non-Hodgkin's).

**Table 1.68:** Diseases associated with lymphadenopathy**1. Infectious diseases**

- a. *Viral infections*, e.g. infectious mononucleosis syndromes (EBV, CMV), infectious hepatitis, HIV, herpes infections.
- b. *Bacterial infections*, e.g. streptococcal, staphylococcal, salmonella, brucella, pasteurella pestis.
- c. *Fungal infections*, e.g. histoplasmosis, coccidioidomycosis
- d. *Mycobacterial infections*, e.g. tuberculosis, leprosy.
- e. *Spirochetal*, e.g. syphilis, leptospirosis
- f. *Parasitic*, e.g. toxoplasmosis

**2. Immunological disease**

- Rheumatoid arthritis, juvenile rheumatoid arthritis
- Mixed connective tissue disorders
- SLE, dermatomyositis
- Sjogren's syndrome
- Serum sickness
- Drug hypersensitivity, e.g. diphenhydantoin, gold, hydralazine, carbamazepine, allopurinol, etc.
- Graft vs host disease
- Silicone – associated
- Primary biliary cirrhosis

**3. Neoplastic disorders**

- Primary, e.g. leukaemia, lymphomas
- Metastatic or secondary, e.g. breast, lung, thyroid, stomach

**4. Lipid storage diseases**, e.g. Gaucher's disease, Niemann–Pick's disease, Tangier disease.**5. Miscellaneous**

- Amyloidosis
- Sarcoidosis
- Histiocytosis X
- Inflammatory pseudotumour of lymph node
- Mucocutaneous lymph node syndrome (Kawasaki's disease)
- Castlemen's disease (giant lymph node hyperplasia)
- Familial mediterranean fever

**263. What is differential diagnosis of localised or regional adenopathy?**

**Ans.** The site of localised lymphadenopathy may provide a useful clue to the cause (Table 1.69).

**264. How will you proceed to diagnose a case of lymphadenopathy?**

**Ans.** Points to be noted in lymphadenopathy are:

- Site
- Size and shape
- Consistency or texture (soft, firm, hard, rubbery)
- Tenderness (present or absent)
- Fixation (mobile or fixed to the underlying or overlying structures)

**Table 1.69:** Site of involvement of lymph node as a clue to the diagnosis

Site	Cause(s)
Occipital adenopathy	Scalp infection
Preauricular adenopathy	Conjunctival infection
Left supraclavicular lymph node (Virchow's gland)	Metastasis from gastric or gastrointestinal cancer
Supraclavicular nodes enlargement	<ul style="list-style-type: none"> <li>• Tuberculosis, sarcoidosis, toxoplasmosis</li> <li>• Metastases from lung, breast, testis or ovary</li> </ul>
Axillary lymphadenopathy	<ul style="list-style-type: none"> <li>• Injuries of upper limb</li> <li>• Localised infection of ipsilateral upper extremity</li> <li>• Malignancies, e.g. melanoma, lymphoma and breast carcinoma</li> </ul>
Inguinal lymphadenopathy	<ul style="list-style-type: none"> <li>• Infections or trauma of lower extremity, plague</li> <li>• Sexually transmitted diseases, e.g. lymphogranuloma venereum, primary syphilis, genital herpes or chancroid</li> <li>• Lymphomas and metastases from rectum and genitalia</li> </ul>
Thoracic lymph nodes (hilar lymphadenopathy)	<ul style="list-style-type: none"> <li>• Tuberculosis, sarcoidosis, fungal infection</li> <li>• Lymphoma, malignancy lung with metastases in lymph node</li> </ul>
Abdominal lymphadenopathy (retroperitoneal, para-aortic)	<ul style="list-style-type: none"> <li>• Tuberculosis (mesenteric lymphadenitis)</li> <li>• Lymphoma</li> <li>• Metastases from the abdominal viscera</li> </ul>

- Matted or discrete
- Local temperature is raised or not (hot or cold)
- Change in colour of the skin – *sacrofuloderma*
- Margins – defined or ill-defined
- Associated features
- Associated splenomegaly or hepatosplenomegaly.

### 265. What are the causes of painful tender lymph nodes?

**Ans.** The causes are:

1. *Acute inflammation or infection*
  - Viral – infectious mononucleosis
  - Bacterial – pyogenic infections, tuberculosis, brucellosis, plague, diphtheria, leprosy
  - Parasitic – toxoplasmosis
  - Fungal infections
2. *Immunological causes*
  - SLE and other collagen vascular disorders
  - Rheumatoid arthritis
3. *Neoplastic*
  - Acute leukaemia (lymphoblastic)
  - Metastases in the lymph node

*Note* Tenderness or pain in lymphadenopathy is due to stretching of the capsule as a result of rapid or sudden enlargement of lymph node due to any cause

### 266. What are the causes of fixation of the lymph nodes to surrounding structures?

**Ans.** The causes are:

- Tuberculosis
- Malignancy or metastases in the lymph nodes

### 267. What are the causes of lymphadenopathy with splenomegaly?

**Ans.** The causes are:

- Infectious mononucleosis
- Lymphoma
- Acute or chronic leukaemia especially lymphatic
- Sarcoidosis
- Collagen vascular disorders, e.g. SLE, RA
- Toxoplasmosis
- Cat-scratch disease
- Disseminated or miliary tuberculosis.

### 268. How will you investigate for a case with lymphadenopathy?

**Ans.** The investigations are done to find out the cause. They are planned depending on the site and type of involvement.

1. *Complete hemogram.* Presence of anaemia (low haemoglobin) with lymphadenopathy indicates chronic infections, chronic disorders (e.g. rheumatoid

arthritis, or felty syndrome, SLE) or malignant disease (e.g. leukaemias, lymphomas, metastasis). Anaemia in these conditions is normocytic and normochromic.

Complete blood count can provide useful data for diagnosis of acute or chronic leukaemia (leucocytosis with immature cells), infectious mononucleosis (leucopenia), lymphoma, pyogenic infections (leucocytosis) or immune cytopenias in illness like SLE.

Raised ESR suggests tuberculosis, rheumatoid arthritis, SLE, acute infections.

## 2. Serological tests

- To demonstrate antibodies specific to components of EBV, CMV, HIV and other viruses, toxoplasma gondii, brucella
- VDRL test for syphilis
- Antinuclear antibodies, LE cell phenomenon and anti-DNA antibodies for SLE and other collagen vascular disorders
- Rheumatoid factor for rheumatoid arthritis

## 3. Blood culture for causative organism in acute infections

## 4. Chest X-ray. It will reveal hilar or mediastinal lymph node enlargement, if any. Unilateral hilar lymph node enlargement usually suggests malignancy lung or tuberculosis; bilateral enlargement indicates sarcoidosis, histoplasmosis or lymphoma.

The chest X-ray will also confirm the involvement of lung in acute infections, tuberculosis, and primary or metastatic lung tumours.

## 5. Imaging techniques (ultrasound, colour Doppler ultrasonography, CT scan, MRI) have been employed to differentiate benign from malignant lymph nodes especially in head and neck cancer. These techniques

especially USG have been used to demonstrate the ratio of long (L) axis to short (S) axis in cervical nodes. An L/S ratio of  $<2.0$  is used to distinguish between benign and malignant lymph nodes in head and neck cancer and has sensitivity and specificity of 95%. This ratio has greater sensitivity and specificity than palpation or measurement of either the long or short axis alone.

Ultrasonography or CT scan abdomen will also reveal lymph node enlargement in the chest and abdomen (mesenteric, para-aortic) which are not palpable on per abdomen examination. These imaging techniques are used for staging lymphomas and to detect enlargement of spleen before it becomes palpable.

## 6. Lymph node biopsy. The indications for lymph node biopsy are imprecise inspite of so many studies done in this regard, yet it remains a valuable diagnostic tool. It is useful to carry out lymph node biopsy;

- If history and physical findings suggest a malignancy, i.e. a solitary, hard, nontender cervical node in an older patient who is chronic smoker.
- Supraclavicular lymphadenopathy
- Generalised or solitary lymphadenopathy with splenomegaly suggestive of lymphoma.

Fine needle aspiration should not be performed as the first diagnostic procedure. Most diagnoses require more tissue than obtained on FNAC.

- A young patient with peripheral lymphadenopathy (lymph node size  $>2$  cm in diameter with abnormal chest X-ray.

Generally, any lymph node  $>2$  cm in diameter should be biopsied for aetiological diagnosis.



## CASE 22: SPLENOMEGALY

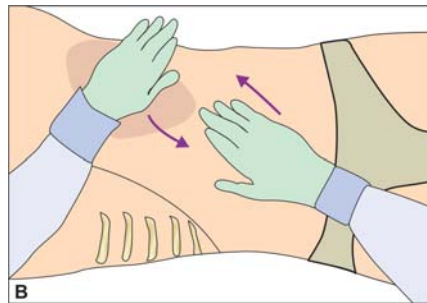
A female patient (Fig. 1.22A) presented with a mass in the left hypochondrium and associated dragging pain. There was no history of fever, haematemesis or bleeding from any site. She gave history of weakness and exertional dyspnoea. No history of jaundice or drug intake or prolonged cough in the past.

### Points to be Noted in History

- History of fever, sore throat bleeding from nose, mouth, rectum, etc.
- History of piles and/or haematemesis, jaundice
- History of palpitation, dyspnoea, orthopnoea and PND
- Any history of weight loss, fatigue, night sweats
- Past history of jaundice haematemesis, RHD, tuberculosis, malignancy.

### General Physical Examination

- Face for puffiness or oedema
- Mouth for any evidence of infection, ulceration or excoriation or thrush
- Tongue—look for anaemia
- Neck for lymphadenopathy, JVP, thyroid enlargement
- Pulse, BP, respiration and temperature
- Hands for clubbing, splinter haemorrhage, Roth's spots, gangrene
- Feet for oedema.



**Figs 1.22A and B:** A. A patient with massive ( $> 8$  cm) splenomegaly producing left hypochondriac protrusion; B. Method of palpation for splenomegaly (diagram)

### Clinical Presentations

- Splenomegaly may be asymptomatic and without any disease
- Pain and dragging sensation in the left upper quadrant is a common presentation with chronic splenomegaly. Massive splenomegaly can produce early satiety.
- Acute pain in left upper quadrant may result due to acute splenomegaly with stretching of the capsule, infarction (vascular occlusion of splenic vessels in subacute bacterial endocarditis, sickle cell crisis in children) or inflammation (perisplenitis) of the spleen.
- Rupture of the spleen either from trauma or infiltrative disease means rupture of the capsule with intraperitoneal bleeding, may result in shock, hypotension and death. The rupture itself may be painless. The disease associated with rupture of spleen include; *chronic leukaemias, myelofibrosis, congestive splenomegaly.*

### Systemic Examinations

#### I. Examination of abdomen

- Look for any swelling or protuberance of abdomen especially in left hypochondria region
- Palpate the abdomen for enlargement of spleen, liver and lymph nodes. In case spleen or liver is enlarged, note the details of characteristics of liver or splenic mass
- Percussion over the mass. In a case with splenomegaly percuss for Traube's area for dullness. In case of hepatomegaly, define the upper border of liver dullness on percussion and record the liver span by measurement
- Auscultate over the mass for any rub, bruit etc.

#### II. Examination of respiratory system

- Examine for signs of hilar lymphadenopathy (e.g. superior mediastinal syndrome—read short case discussion on it)
- Look for signs of LHF

#### III. Examination of CVS

- Inspect the precordium for any precordial bulge or cardiac enlargement
- Palpate the apex for any evidence of derivation/shift or thrill
- Auscultate the heart for sounds, murmurs or rub and for evidence of LVF or pericardial disease especially pericardial effusion or rheumatic valvular disease

#### IV. Examination of Blood

- Look for signs of haemorrhage or bleeding into the skin or organ
- Elicit sternal tenderness.



**269. How do you define splenomegaly?**

**Ans.** Splenomegaly literally means enlargement of spleen. Palpable spleen means its enlargement 2 to 3 times than normal. Normal spleen measures 12 × 7 cm on ultrasonography, radionuclide scan and CT scan. Spleen is palpable in 1-3% normal individuals without any cause. Its incidence in normal population in New Guinea has been reported to be very high (upto 60%). Spleen is said to be enlarged if its span on USG is > 14 cm.

**270. What are the causes of splenomegaly?**

**Ans.** Many of the diseases associated with splenomegaly are listed in Table 1.70. They are grouped according to presumed basic mechanisms responsible for spleen enlargement.

The differential diagnostic possibilities narrow down when the spleen is massively enlarged (>8 cm below the costal margin and its dried weight is >1000 g) (Table 1.71).

**271. What are the causes of palpable spleen without is enlargement?**

**Ans.** Normally spleen may be palpable without being enlarged in;

- Some children below 10 years of age
- Thin lean persons
- COPD (spleen is pushed down by hyperinflated lung)
- Visceroptosis (drooping of viscera including spleen)

**272. What are causes of splenomegaly with fever?**

**Ans.** Spleen enlarges within few days to few weeks of fever

- Bacterial endocarditis
- Acute malaria
- Kala-azar
- Tuberculosis
- Infectious mononucleosis
- Histoplasmosis
- Typhoid fever
- Acute leukaemia
- Lymphoma
- SLE
- Haemolytic crisis

**273. What are the causes of splenomegaly with anaemia?**

**Ans.** The causes are:

- Bacterial endocarditis

**Table 1.70:** Diseases associated with splenomegaly

- 1. Infective disorders (immune system hyperplasia)**
  - a. *Bacterial*, e.g. endocarditis, septicaemia, tuberculosis, salmonella
  - b. *Viral*, e.g. hepatitis, AIDS, infectious mononucleosis
  - c. *Protozoal*, e.g. malaria, leishmania, trypanosomiasis
  - d. *Spirochetal*, e.g. syphilitic
  - e. *Fungal*, e.g. histoplasmosis
- 2. Inflammatory/granulomatous disorders (disordered immune regulation)**
  - Rheumatoid arthritis, Felty's syndrome
  - Collagen vascular disorders, e.g. SLE
  - Immune haemolytic anaemia
  - Sarcoidosis
  - Immune thrombocytopenias
- 3. Congestive splenomegaly (abnormal splenic or portal blood flow)**
  - Hepatic vein thrombosis (Budd-Chiari's syndrome)
  - Portal vein obstruction/ thrombosis
  - Congestive heart failure
  - Pericardial effusion
  - Primary portal hypertension (Banti's spleen)
  - Secondary portal hypertension
  - Splenic vein thrombosis
  - Hepatic schistosomiasis
- 4. Diseases associated with haemolysis (reticulo-endothelial system hyperplasia)**
  - Spherocytosis
  - Ovalocytosis
  - Paroxysmal nocturnal haemoglobinuria
  - Sickle cell disease
  - Thalassaemia
- 5. Infiltrative diseases of the spleen**
  - A. Intra or extracellular depositions**
    - Amyloidosis
    - Fatty infiltration, e.g. Gaucher's and Niemann – Pick's disease
    - Hyperlipidaemia
    - Hurler's syndrome
    - Tangier disease
  - B. Benign and malignant cellular infiltration**
    - Leukaemias (acute and chronic, lymphoid, myeloid, monocytic)
    - Lymphomas (Hodgkin's and non-Hodgkin's)
    - Myeloproliferative disorders (e.g. polycythaemia rubra vera)
    - Metastatic tumours
    - Eosinophilic granuloma
    - Histiocytosis X
    - Splenic cysts
- 6. Miscellaneous**
  - Iron deficiency anaemia
  - Idiopathic splenomegaly
  - Hyperthyroidism
  - Berylliosis

**Table 1.71:** Causes of various grades of splenomegaly

Mild	Moderate	Massive
<ul style="list-style-type: none"> <li>• Congestive heart failure</li> <li>• Bacterial endocarditis</li> <li>• Typhoid fever</li> <li>• SLE</li> <li>• Acute malaria (chronic malaria produces massive splenomegaly)</li> <li>• Rheumatoid arthritis</li> </ul>	<ul style="list-style-type: none"> <li>• Cirrhosis of liver with portal hypertension</li> <li>• Hepatitis</li> <li>• Haemolytic anaemia</li> <li>• Infectious mononucleosis</li> <li>• Amyloidosis</li> <li>• Splenic abscess or cyst</li> <li>• Idiopathic thrombocytopenic purpura</li> </ul>	<ul style="list-style-type: none"> <li>• Chronic malaria and kala-azar</li> <li>• Chronic myeloid leukaemia (CML)</li> <li>• Myelofibrosis/myelosclerosis</li> <li>• Chronic lymphatic leukaemia (CLL)</li> <li>• Hairy cell leukaemia</li> <li>• Polycythemia rubra vera</li> <li>• Sarcoidosis</li> <li>• Autoimmune haemolytic anaemia</li> <li>• Lymphomas</li> <li>• Gaucher's disease in children</li> </ul>

- Hemolytic anaemia
- Cirrhotic portal hypertension with repeated haematemesis
- Myeloproliferative syndromes
- Malaria
- Felty's syndrome
- SLE
- Rheumatoid arthritis.

**274. What are causes of splenomegaly with jaundice?**

**Ans.** Jaundice may be haemolytic or hepatic

- Cirrhosis of liver
- Acute viral hepatitis (uncommon)
- Acute malaria (*P. falciparum*) due to haemolysis
- Hepatic vein thrombosis (Budd-Chiari syndrome)
- Haemolytic anaemia
- Lymphoma
- Miliary tuberculosis

**275. What are the common causes of fever, lymphadenopathy, splenomegaly with or without rash?**

**Ans.** The conditions are:

- Infectious mononucleosis
- Sarcoidosis
- Acute leukaemia or blast crisis in chronic leukaemia
- SLE
- Lymphoma
- Felty's syndrome

**276. What are the causes of splenomegaly with ascites?**

**Ans.** The causes are:

- Portal hypertension
- Budd-Chiari syndrome
- Lymphoma
- CML
- Viral hepatitis with hepatocellular failure

**277. What are the causes of splenic rub? Where do you hear it? What does it indicate?**

**Ans.** Splenic rub can be heard over the enlarged spleen with stethoscope in conditions associated with splenic infarction (perisplenitis) due to vascular occlusion of spleen. The patient complains of acute left upper quadrant pain abdomen which may radiate to tip of left shoulder. The spleen is enlarged and tender. The causes are:

- Subacute bacterial endocarditis
- Chronic myeloid leukaemia
- Sickle cell anaemia
- Following splenic puncture for diagnosis of kala-azar

Splenic rub is heard over the spleen or left lower chest during respiration

**278. What is hypersplenism? What are its causes?**

**Ans.** Hypersplenism refers to overactivity of the splenic function, has nothing to do with the size of the spleen. It is characterised by a tetrad consisting of;

- Splenomegaly of any size

- Cytopenias/pancytopenias (anaemia, leucopenia and/or thrombocytopenia)
- Normal or hypercellular marrow
- Reversibility following splenectomy

*Causes of Hypersplenisms are:*

- Lymphoma
- Cirrhosis of the liver
- Myeloproliferative disorders
- Connective tissue disorders

Pancytopenia of hypersplenism differs from pancytopenia due to aplastic anaemia by hypercellular or normal bone marrow. It is due to the fact that in hypersplenism, all the formed elements of blood (RBCs, WBCs and platelets) are being destroyed in the spleen which stimulates the bone marrow and makes it hypercellular. On the other hand, in aplastic anaemia, bone marrow is hypocellular due to aplasia or hypoplasia of the marrow elements.

### 279. What are causes of hyposplenism or asplenia?

**Ans.** It refers to virtual absence of spleen (asplenia) or malfunctioning spleen (hyposplenism). It is usually associated with;

- Dextrocardia
- Sickle cell disease leading to multiple infarcts
- Coeliac disease
- Fanconi's anaemia (aplastic anaemia with hypoplasia of spleen, kidney, thymus, etc.)
- Surgical removal of the spleen.
- Splenic irradiation for autoimmune or neoplastic disease.

### 280. How will you investigate a patient with splenomegaly?

**Ans.** The investigations to be done are:

- *Haemoglobin and RBCs count.* Haemoglobin is *low* in thalassemia major, SLE, cirrhotic portal hypertension and *increased* in polycythaemia rubra vera.
- *WBC count.* Granulocyte counts may be *normal*, *decreased* (Felty's syndrome, congestive splenomegaly, aleukaemic leukaemia) or *increased* (infections, or inflammatory disease, myeloproliferative disorders).
- *Other investigations* are same as discussed under hepatosplenomegaly (read them there).

### 281. What are indications of splenectomy (removal of spleen)?

**Ans.** Indications are:

1. For immune-mediated destruction of one or more cellular blood elements, for example, in immune thrombocytopenia
2. For sickle cell crises (splenic sequestration) in young children
3. For correlation (reversibility) of cytopenias in patients with hypersplenism
4. For disease control in patients with splenic rupture.
5. More often splenectomy is performed in stage III and IV of Hodgkin's disease.
6. For symptom control in patients with massive splenomegaly

### 282. What are the clinical manifestations of splenectomy?

**Ans.** These will be:

- Marked variations in size and shape of RBCs (anisocytosis, poikilocytosis)
- Presence of Howell-Jolly bodies (nuclear remnants), Heinz bodies (denatured Hb), basophilic stippling and an occasional nucleated RBC in the peripheral blood.

### 283. What will be the consequences of splenectomy?

**Ans.** The consequences will be:

1. The most serious consequence of splenectomy is predisposition to bacterial infections, particularly with *S. pneumoniae*, *H. influenzae* and some gram-negative enteric organisms. They should be immunised against these organisms. The vaccination recommended are given in the box.
2. The splenectomised patients are more susceptible to a parasitic disease – *babesiosis*, hence, they should avoid visit to areas where the parasite – *Babesia* is endemic.

#### Vaccination before and after splenectomy

The Advisory Committee on Immunisation Practices recommends that pneumococcal vaccine should be administered to all patients before elective splenectomy and a repeat dose of vaccination 5 years later.

The vaccination against *N. meningitidis* should also be given to patients in whom elective splenectomy is planned.

**284. What is Traube's area? What is its significance?**

**Ans.** Normal Traube's area is bounded above by the lung resonance, below the costal margins on the right side by left border of the liver and on the left by the normal splenic dullness. It lies in left lower chest behind 9th, 10th and 11th rib.

- Normally it is resonant because it is occupied by stomach (tympanic note)
- It becomes dull in:
  - Left side pleural effusion
  - Splenomegaly
  - Distended stomach with fluid or solid growth.

**285. What are differences between a splenic and left renal mass?**

**Ans.** Read clinical method vol. I by Prof. SN Chugh.

**286. How will you palpate spleen in the presence of ascites?**

**Ans.** For method of palpation of spleen (Fig. 1.22B), read clinical methods. However, in the presence of ascites, spleen is palpated by dipping method.

**287. What are characteristics of a splenic mass?**

**Ans.** Read Clinical Method in Medicine Vol. I.

**288. What are other causes of mass in left hypochondrium?**

**Ans.** Read Clinical Method in Medicine.

## CASE 23: HEPATOSPLENOMEGALY

The patient (not in picture) presented with gradual onset of fever, malaise, weakness. There was history of masses in the abdomen with dyspnoea, pallor. Patient gave history of taking anti-malarial drug following which the fever subsided.

## Points to be Noted in History

- History of fever or sore throat, jaundice, bleeding from any site
- History of palpitation, breathlessness orthopnoea, PND
- Any history of infection, mouth ulcerations, mouth thrush, excoriation, etc.

## General Physical Examination

Look at

- Face for puffiness, oedema
- Mouth for ulceration, excoriation or thrush
- Tongue for anaemia. Look other sites for anaemia
- Neck for lymph node enlargement, JVP and thyroid enlargement
- Pulse, BP, temperature and respiration
- Hands for koilonychia, platynychia, splinter haemorrhage, clubbing
- Feet for oedema

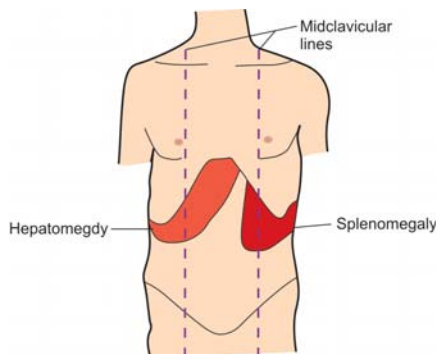


Fig. 1.23: Hepatosplenomegaly—a diagram

## Clinical Presentation of Hepatosplenomegaly

These patients usually present either with dull ache or pain in right and left hypochondrium, but most of the time they may complain of masses in the abdomen (Fig. 1.23).

## Systemic Examination

## I. Abdomen

- Look for any swelling or bulge
- Palpate the masses in the abdomen and describe their characteristics
- Percuss for Traube's area for splenic dullness and define the upper border of the liver for its enlargement and liver span measurement
- Auscultate over the mass(es) for any bruit or rub

## II. CVS examination

- Examine the heart for any enlargement, murmur, sounds or rub
- Look for the signs of valvular heart disease, LVF, SABE and pericardial disease especially pericardial effusion

## III. Examination of blood

- Look for any haemorrhage into the skin or joint or organ
- Examine ocular fundi for haemorrhage

## 289. What are the causes of hepatosplenomegaly?

Ans. The causes are:

1. *Infections*, e.g. malaria, kala azar, typhoid, acute miliary or disseminated tuberculosis, viral hepatitis (occasional) and brucellosis.
2. *Blood disorders*, e.g. haemolytic anaemia, chronic myeloid leukaemia, lymphoma, polycythemia rubra vera, chronic lymphatic leukaemia, acute leukaemias.
3. *Extramedullary erythropoiesis*, e.g. myelofibrosis, myelosclerosis.
4. *Diseases of liver*, e.g. cirrhosis, Budd-Chiari syndrome.
5. *Congestive hepatosplenomegaly*, e.g. pericardial effusion, constrictive pericarditis and congestive cardiac failure (cardiomyopathy)

6. *Infiltrative disorders*, e.g. amyloidosis

7. *Miscellaneous*, e.g. sarcoidosis.

## 290. What is the differential diagnosis of hepatosplenomegaly in an adult?

Ans. The conditions that come into differential diagnosis are discussed below.

*Chronic Malaria:*

The characteristic features are;

- Patient belongs to an endemic zone
- Fever with chills and rigors. Fever may come on alternate days periodically
- Anaemia and mild jaundice may be present if haemolysis occurs
- Massive splenomegaly with moderate hepatomegaly, firm to hard and nontender



- Diagnosis is confirmed by demonstration of the parasite in the peripheral blood.

#### *Chronic Kala-azar*

- Patient belongs to an endemic area
- Double rise or peak in temperature (biphasic pattern) in 24 hours may be present
- Patient is well despite symptoms and signs
- The skin is dry and pigmented
- Hepatosplenomegaly in which spleen is massively enlarged while liver enlargement is moderate. Both are firm and nontender.
- The diagnosis is confirmed by demonstration of LD bodies in buffy coat preparations of blood or in the bone marrow smear or lymph node, liver, or spleen aspirates (splenic puncture).

#### *Thalassaemia (Colley's Anaemia)*

- A hereditary disorder of haemoglobin (haemoglobinopathy) hence, the patient is usually a child or young person with positive family history.
- Stunted growth and mongoloid facies
- Moderate hepatosplenomegaly, nontender, soft to firm
- Severe anaemia and mild jaundice (haemolysis)
- Anaemia is microcytic and hypochromic
- Leg ulcers
- Diagnosis is confirmed by radiological study of skull and presence of abnormal hemoglobin (HbF >2%) on electrophoresis.

#### *Haemolytic Anaemia*

- Gradual onset of anaemia
- Mild jaundice
- Dark coloured urine and stool during an episode of haemolysis
- Moderate nontender hepatosplenomegaly
- Positive tests for haemolysis will confirm the diagnosis.

#### *Chronic Myeloid Leukaemia*

- Patient is middle aged or old aged person with slow onset of symptoms
- The presenting symptoms are dragging pain in left hypochondrium due to massive splenomegaly and profound weakness, weight loss and sweating.

- Moderate anaemia
- Hepatosplenomegaly due to extramedullary erythropoiesis. The spleen is massively enlarged (>8 cm), firm to hard and occasionally a splenic rub may be present if a splenic infarct occurs. The liver is moderately enlarged.
- Sternal tenderness is present
- Diagnosis is confirmed by presence of anaemia, high WBC count (in lacs) with immature WBCs (myelocytes, metamyelocytes and promyelocytes with few myeloblasts (<10%).

#### *Lymphoma*

- Painless progressive enlargement of cervical, axillary and inguinal lymph nodes, discrete, firm, but rubbery in consistency in Hodgkin's lymphoma.
- Fever, weight loss, weakness, pruritus with drenching night sweats may occur
- Moderate hepatosplenomegaly
- Moderate anaemia
- Eosinophilia present
- Lymph node biopsy is diagnostic.

#### *Cirrhosis (Postnecrotic) of Liver*

- Symptoms and signs of chronic liver disease, e.g. weakness, malaise, muscle wasting.
- Past history of jaundice, e.g. viral hepatitis
- Features of portal hypertension, e.g. haematemesis, melena, splenomegaly, fetor hepaticus, caput medusae or distended veins on the abdomen with ascites.
- Moderate hepatosplenomegaly, firm, nontender
- Diagnosis is made by oesophageal varices, splenoportal venography and liver biopsy
- Presence of other stigmata of cirrhosis (Read case discussion on Cirrhosis of Liver).

#### *Budd-Chiari syndrome (Hepatic Vein Thrombosis)*

- Gradual onset of symptoms
- The triad of signs and symptoms includes; gross intractable ascites, jaundice and massive tender hepatomegaly.
- Splenomegaly will occur along with hepatomegaly in patients who develop portal hypertension. Other signs of portal hypertension will also appear.

- Peripheral oedema is present if there is inferior vena cava obstruction
- The diagnosis is confirmed on (i) *Doppler ultrasound* (obliteration of hepatic veins, reversed flow or associated portal vein thrombosis), (ii) *CT scan* showing enlargement of caudate lobe, (iii) *hepatic venography* showing obstruction of hepatic veins and (iv) *liver biopsy* demonstrates centrilobular congestion with fibrosis.

### Enteric Fever

- History of fever which rises in step-ladder pattern, headache, diarrhoea or constipation, epistaxis, cough, rose spots over skin and relative bradycardia.
- The tongue is red (angry-looking)
- Mild to moderate hepatosplenomegaly which is soft and tender, appears on 7th to 10th of fever
- Diagnosis is confirmed by blood culture and rising titres of antibodies on widal test.

### Myelofibrosis/Myelosclerosis

- It may be primary or secondary to toxins, malignant infiltration of bone marrow, lymphoma or irradiation.
- Massive splenomegaly with moderate hepatomegaly due to extramedullary hematopoiesis. Splenic rub may be present occasionally.
- Leucoerythroblastic blood picture with high platelet count
- Ground glass appearance of bones on X-ray
- Bone marrow examination may yield a “dry tap”, hence, trephine biopsy is needed to confirm the diagnosis.

### Miliary Tuberculosis

- Gradual onset of symptoms with fever, anorexia, weight loss and night sweats
- Cough, breathlessness, headache, hemoptysis may be present
- Tachycardia, tachypnoea with few chest signs such as fine crackles.
- Mild to moderate hepatosplenomegaly
- Signs of meningitis may be present. CSF shows changes of meningitis

- Fundus examination may reveal choroid tubercles (25% cases)
- Leucocytosis is absent
- Montoux test is negative
- Chest X-ray shows miliary mottling shadows widely distributed in both the lungs
- Sputum examination may or may not be positive.

### Amyloidosis

- It is secondary to suppurative lung disease (lung abscess, bronchiectasis), Crohn's disease, multiple myeloma, rheumatoid arthritis, leprosy
- Macroglossia may be present
- Mild to moderate hepatosplenomegaly
- Evidence of renal involvement, i.e. massive proteinuria (nephrotic syndrome)
- Other associated involvement include malabsorption, lymphadenopathy, peripheral neuropathy, cardiomyopathy
- The diagnosis is confirmed on liver, gingival or rectal biopsy.

### 291. What are the causes of fever with hepatosplenomegaly?

**Ans.** The presence of fever indicates infection or inflammation, hence, may be associated with leucocytosis or leucopenia. The causes are:

- Parasitic infections, e.g. malaria, kala-azar
- Bacterial infection, e.g. enteric fever, brucellosis, miliary tuberculosis
- Viral infection, e.g. acute lupoid hepatitis
- Acute leukaemia and lymphoma
- Haemolytic crisis.

### 292. What are the causes of hepatosplenomegaly with lymphadenopathy?

**Ans.** The liver, spleen and lymph nodes constitute the lymphoreticular system, hence, the disorders involving this system will produce their enlargement such as;

- Acute leukaemia especially ALL in children
- Lymphoma (Hodgkin's and non-Hodgkin's)
- Miliary tuberculosis
- Sarcoidosis
- AIDS
- Infectious mononucleosis
- Collagen vascular disorder, e.g. SLE.

**293. What are the causes of hepatosplenomegaly with jaundice?**

**Ans.** Jaundice in presence of hepatosplenomegaly occurs either due to decompensation of liver or infection of the liver or due to haemolysis. The causes are:

- Cirrhosis of liver with decompensation
- Budd-Chiari syndrome (hepatic vein thrombosis)
- Lupoid hepatitis
- Malaria (falciparum infection producing haemolysis)
- Lymphoma (especially non-Hodgkin's)
- Miliary tuberculosis.

**294. What are conditions that produce hepatosplenomegaly with ascites?**

**Ans.** Ascites in the presence of hepatosplenomegaly may be a sign of portal hypertension or hepatocellular failure or may be due to malignant infiltration of the peritoneum. The causes are:

- Cirrhosis liver with portal hypertension
- Budd-Chiari syndrome with portal hypertension
- Chronic myeloid leukaemia
- Lymphoma (non-Hodgkin's)
- Subacute or lupoid hepatitis with or without hepatocellular failure.

**295. What are the causes of congestive hepatosplenomegaly?**

**Ans.** The conditions are:

- Congestive heart failure
- Pericardial effusion/Constrictive pericarditis
- Budd-Chiari syndrome
- Extramedullary erythropoiesis, e.g. chronic myeloid leukaemia, myeloid metaplasia.

**296. How will you investigate a case of hepatosplenomegaly?**

**Ans.** The investigations to be done are:

1. **TLC and DLC.** Leucocytosis indicates pyogenic infections, polycythaemia and leukaemia while leucopenia occurs in malaria, enteric fever, kala-azar. Pancytopenia indicates hypersplenism.
2. **Peripheral blood film** for MP, kala-azar (LD bodies) and haemolytic anaemia (abnormal type of cells) or other types of anaemia. Reticulocytosis indicates haemolytic anaemia. Presence of premature WBCs indicate leukaemia (acute or chronic).

3. **Blood culture** for enteric

**4. Special tests**

- Paul-Bunnell test for infectious mononucleosis
- Widal test for typhoid and brucella
- Serum bilirubin for jaundice
- Aldehyde test for kala azar
- Tests for haemolysis, e.g. osmotic fragility, Coomb's test

**5. Radiology**

- Chest X-ray for:
  - miliary tuberculosis (miliary mottling)
  - lymphoma and sarcoidosis (mediastinal widening due to mediastinal lymphadenopathy)
- X-ray bones
  - Skull ('Hair on end' appearance in thalassaemia)
  - Long bones, e.g. expansion of lower ends of the bone in Gaucher's disease. Increased density of the bones in myelofibrosis or myeloid sclerosis

**6. USG of abdomen**

- To confirm hepatosplenomegaly
- To detect the presence of ascites, portal hypertension (portal vein diameter >14 mm) and dilated venous collaterals.
- To detect echogenic pattern of the liver (heterogeneous pattern indicates cirrhosis)

**7. Biopsy**

- Lymph node biopsy for tuberculosis, sarcoidosis and lymphoma
- Liver biopsy for cirrhosis of the liver and amyloidosis
- Bone marrow biopsy (trephine) for myelofibrosis
- Bone marrow aspiration for leukaemia, lymphoma Gaucher's disease and, hypersplenism (pancytopenia with hypercellular marrow), splenic aspirate for kala-azar.

**8. Skin tests**

- Mantoux test for tuberculosis
- Kveim test for sarcoidosis (not done now-a-days)

**9. CT scan abdomen**

- To detect lymph node enlargement
- To confirm the findings on USG
- To stage the lymphoma.

**CASE 24: THYROTOXICOSIS**

The young female (Fig. 1.24) presented with palpitation, drenching sweats and a neck swelling. There was history of off and on loose motions and she had lost 3 kg weight past 1 month.

Examination of the patient revealed tachycardia, rapid collapsing pulse, exophthalmose, staring look, lid lag and lid retraction. The thyroid was enlarged with smooth texture. A bruit was heard over the thyroid.

**Points to be Noted in History**

- Record the chief complaints in chronological order and describe their details
- Ask for any restlessness, irritability, behavior change, hyperexcitability
- Ask for weight loss, increased appetite, nausea, vomiting, diarrhoea
- Ask for palpitation, breathlessness, heat intolerance
- Ask for menstrual irregularity, loss of libido, gynaecomastia, etc

**General Physical Examination**

- Look at the face for perspiration, staring look, exophthalmose, loss of frowning or wrinkling
- Look for eye signs of thyrotoxicosis, e.g. lid lag, lid retraction, exophthalmos, ophthalmoplegia, loss of accommodation
- Examine neck for thyroid enlargement. Describe the size, shape, measurement, palpate thyroid for smooth texture or nodularity and auscultate for bruit. Examine the neck veins for JVP
- Record the pulse, BP, temperature and respiration
- Look at the hands for tremors, clubbing, moistness, perspiration, warmth, palmar erythema
- Examine feet for oedema and legs for pretibial myxoedema



**Fig. 1.24: Graves' disease**

**Clinical Presentations**

- Patients usually present with goitre (swelling in the neck) and symptoms of thyrotoxicosis. These are cases of Graves' disease and nodular goitre (Fig. 1.24).
- Patients may present with unexplained weight loss inspite of good appetite, without any diarrhoea or malabsorption. These are usually cases of occult thyrotoxicosis.
- Patients may present with arrhythmias (atrial fibrillation) especially old patients
- The young patients present with symptoms of sympathetic overactivity, i.e. palpitations, nervousness, sweating, insomnia, tremulousness, weakness, menstrual irregularity (in females)
- Patients may present with psychiatric manifestations, e.g. irritability, anger, hyperactivity, depression

*Note:* Patients present in variety of ways because thyrotoxicosis disturbs the general metabolism in such a way that every system is affected and patient may present with symptoms related to any system.

**Systemic Examination**

- I. CVS examination
  - Inspect the apex beat and look for cardiac enlargement
  - Palpate the apex beat, define its location and other characters
  - Percuss the heart for cardiomegaly
  - Auscultate the heart for third heart sound, murmurs(s) or any other abnormal sound or rub
- II. Respiratory system
  - Examine for crackles and rales for LVF
- III. Nervous system
  - Higher function testing for psychosis
  - Abnormal movements, e.g. tremors, choreoathetosis
  - Examine for peripheral neuropathy, proximal myopathy, etc.



**Table 1.72:** Causes of thyrotoxicosis

Common (>95%)	Less common (3-5%)	Rare (<1%)
<ul style="list-style-type: none"> <li>Graves' disease</li> <li>Multinodular goitre</li> <li>Autonomously functioning solitary thyroid nodule</li> </ul>	<ul style="list-style-type: none"> <li>Thyroiditis, e.g. subacute (de Quervain's and postpartum)</li> <li>Drug-induced (e.g. amiodarone, radioactive contrast media or iodine prophylaxis programme)</li> <li>Factitious (self-induced)</li> <li>Struma ovarii</li> </ul>	<ul style="list-style-type: none"> <li>Pituitary or ectopic TSH by a tumour</li> <li>Thyroid carcinoma</li> </ul>

**297. What is the clinical diagnosis of the patient in picture?**

**Ans.** The young female has symptoms and signs suggestive of thyrotoxicosis with diffuse thyroid enlargement. The probable diagnosis is Grave's disease.

**298. How do you define thyrotoxicosis?**

**Ans.** Thyrotoxicosis implies a state of hyperthyroidism in which the thyroid hormone is toxic to the tissues producing clinical features; while hyperthyroidism simply implies excessive thyroid function. However, both are not synonymous, yet are used interchangeably.

**299. What is Graves' disease?**

**Ans.** It is an autoimmune disorder characterised by hyperthyroidism, diffuse goitre, ophthalmopathy and dermopathy (pretibial myxedema) and thyroid acropachy (clubbing of fingers). A thyroid scan and antithyroid antibodies (TPO, TRAb) are diagnostic.

**300. What are the causes of thyrotoxicosis?**

**Ans.** Causes of thyrotoxicosis are described in Table 1.72.

**301. What are symptoms and signs of thyrotoxicosis?**

**Ans.** See the Table 1.73. The symptoms and signs are due to sympathetic stimulation induced by excess of thyroid hormones.

**302. How do you classify the eye changes in Graves' disease?**

**Ans.** Many scoring systems have been used to gauge the extent and severity of orbital changes in Graves' disease. As a mnemonic, the NOSPECS scheme is used to class the eye signs as follows;

- o = No sign or symptom

- 1 = Only sign (lid lag or retraction), no symptoms
- 2 = Soft tissue involvement (pretibial myxoedema)
- 3 = Proptosis (>22 mm)
- 4 = Extraocular muscle involvement (diplopia)
- 5 = Corneal involvement
- 6 = Sight loss

**303. What is pretibial myxoedema?**

**Ans.** Pretibial myxoedema is a sign of Graves' disease. The name justifies the site of skin changes, i.e. over the anterior and lateral aspects of the lower leg in front of tibia. The typical skin change is noninflamed, indurated, pink or purple colour plaque giving an "orange-skin" appearance. Nodular involvement can uncommonly occur.

**304. What is the differential diagnosis of thyrotoxicosis?**

**Ans.** The two common conditions causing thyrotoxicosis are compared in the Table 1.74.

**305. How will you investigate a case of thyrotoxicosis?**

**Ans.** The investigations to be performed are:

- Measurement of radioactive iodine uptake.** It is increased.
- Thyroid hormones.** The total or free T3 and T4 are increased while TSH is decreased in primary thyrotoxicosis (Graves' disease or MNG); while all the three are increased in secondary (pituitary or ectopic) thyrotoxicosis
- Ultrasound of thyroid** will demonstrate either the diffuse (Graves' disease) or multinodular goitre.
- Thyroid scan.** A radionuclide scan of thyroid either by  $^{131}\text{I}$  or  $^{99\text{m}}\text{Tc}$  will demonstrate functioning thyroid



**Table 1.73:** Symptoms and signs of Grave's disease or hyperthyroidism

1. <b>Goitre</b> (e.g. diffuse or nodular)	<ul style="list-style-type: none"> <li>Diffuse goitre indicates Grave's disease</li> <li>Nodularity indicates toxic nodular (single or multiple) goitre</li> </ul>
2. <b>Gastrointestinal</b>	<ul style="list-style-type: none"> <li>Weight loss in spite of good appetite</li> <li>Vomiting</li> <li>Diarrhoea or steatorrhoea</li> </ul>
3. <b>Cardiovascular</b>	<ul style="list-style-type: none"> <li>High resting pulse rate or tachycardia</li> <li>Good volume pulse with wide pulse pressure (&gt; 60 mmHg)</li> <li>Exertional dyspnoea</li> <li>Arrhythmias (atrial fibrillation is common)</li> <li>Precipitation of angina in a patient</li> <li>With ischaemic heart disease or cardiac failure</li> <li>Systolic hypertension</li> </ul>
4. <b>Neuromuscular</b>	<ul style="list-style-type: none"> <li>Nervousness, irritability</li> <li>Restlessness, psychosis</li> <li>Tremors of hands</li> <li>Muscular weakness mostly proximal</li> <li>Exaggerated tendon reflexes</li> </ul>
5. <b>Dermatological</b>	<ul style="list-style-type: none"> <li>Perspiration (moist hands, increased sweating or hyperhidrosis). Warm and vasodilated peripheries</li> <li>Clubbing of fingers (rare)</li> <li>Loss of hair</li> <li>Pre-tibial myxoedema</li> <li>Redness of palms (palmar erythema)</li> <li>Thyroid acropachy</li> </ul>
6. <b>Reproductive</b>	<ul style="list-style-type: none"> <li>Menstrual irregularity (amenorrhoea is common)</li> <li>Abortions</li> <li>Infertility</li> <li>Loss of libido or impotence</li> </ul>
7. <b>Ophthalmological</b>	<ul style="list-style-type: none"> <li>Lid lag or lid retraction</li> <li>Wide palpebral fissure</li> <li>Diplopia or ophthalmoplegia</li> <li>Staring look</li> <li>Exophthalmos</li> <li>Excessive watering of eyes</li> </ul>
8. <b>Miscellaneous</b>	<ul style="list-style-type: none"> <li>Heat intolerance</li> <li>Out burst of anger</li> <li>Excessive thirst</li> <li>Fatiguability or apathy</li> </ul>

tissue. It will show diffuse increased uptake in Graves' disease but increased or decreased uptake in multinodular goitre. A **hot nodule** means increased uptake while **cold nodule** indicates decreased

**Table 1.74:** Differential diagnosis of thyrotoxicosis

Feature	Graves' disease	Toxic multinodular goitre
• Age	Young age	Old age
• Sex	Common in females	Common in females
• Goitre	Diffuse, firm, smooth. Bruit is heard commonly	Nodular, firm to hard, irregular surface. No bruit
• Eye signs	Common	Uncommon
• Dermopathy (pretibial myxoedema)	May occur	Does not occur
• Severity of thyrotoxicosis	Moderate to severe	Mild to moderate
• Atrial fibrillation	Common	More common
• Compressive symptoms	Uncommon	Common
• Cause	Autoimmune, may be associated with other autoimmune diseases	Autonomous
• Treatment of choice	Drug therapy	Surgery or radioactive iodine

uptake. Thyroid scan will also detect an ectopic thyroid tissue in the neck or chest.

5. **Antithyroid antibodies.** Antithyroid antibodies are detected in Graves' disease and Hashimoto's thyroiditis. TRAb antibodies and TPO antibodies are raised in Graves' disease.
6. **Needle biopsy** of the thyroid is done in MNG to detect underlying malignancy.
7. **Other tests** such as ECG for tachycardias and arrhythmias.
  - CT scan or MRI, TSH suppression tests for pituitary origin of thyrotoxicosis.
8. **Other biochemical abnormalities** are; (i) raised bilirubin and transferases, (ii) raised calcium and glycosuria or impaired glucose tolerance. These are due to other autoimmune diseases associated with it.

### 306. What are eye signs in Graves' disease?

**Ans.** Followings are the symptoms and signs of eye involvement in thyrotoxicosis;

- Grittiness, excessive lacrimation
- Chemosis
- Exophthalmos or proptosis, corneal ulceration

- Lid retraction, lid lag
- External ophthalmoplegia, diplopia
- Papilloedema, loss of visual acuity.

**307. Name the other autoimmune diseases associated with thyrotoxicosis.**

**Ans.** These are:

- Diabetes mellitus
- Hyperparathyroidism
- Chronic active hepatitis
- Autoimmune haemolytic anaemia

**308. What is subclinical hyperthyroidism?**

**Ans.** In this condition, the serum  $T_3$  and  $T_4$  are normal and lie in the upper limit of their respective reference range and the serum TSH is undetectable. This combination is found in patients with nodular goitre. These patients are at increased risk of atrial fibrillation and osteoporosis, hence, the consensus view is to treat such cases with  $^{131}\text{I}$ . As these cases can transform to overt hyperthyroidism, therefore, annual review is mandatory.

**309. What is thyroiditis (hyperthyroidism with reduced iodine uptake)?**

**Ans.** In patients with hyperthyroidism, the RAIU is usually high but a low or negligible uptake of iodine occurs in some rare causes of hyperthyroidism such as thyroiditis (subacute or postpartum). If a radioactive iodine uptake (RAIU) test is not routinely performed in patients with hyperthyroidism, such cases are likely to be missed and inappropriate treatment may be given.

1. *Subacute (de Quervain's) thyroiditis.* It is a viral – induced (coxsackie, mumps, adenovirus) thyroiditis in which there is release of colloid and thyroid hormones into circulation leading to hyperthyroidism.

It is characterised by fever, pain in the region of thyroid gland which may radiate to angle of the jaw and the ears, made worse by swallowing, coughing and movements of neck. The thyroid gland is enlarged and tender. It is seen in young females 20-40 years.

The thyroid hormones levels are high for 4-6 weeks but RAIU is low indicating transient hyperthyroidism which is followed by asymptomatic hypothyroidism and finally erythyroid state is achieved with full recovery within 3-6 months. No

treatment is required except steroids and betablockers for initial period of hyperthyroidism.

2. *Postpartum thyroiditis.* It is subacute autoimmune thyroiditis occurring during postpartum period or within 6 month of delivery. These women exhibit biochemical disturbances of thyroid function reflecting hyperthyroidism, hypothyroidism and hyperthyroidism followed by hypothyroidism lasting for few weeks. These patients have antithyroid peroxidase (TPO) antibodies in the serum in early pregnancy. Thyroid biopsy shows lymphocytic thyroiditis. These patients are asymptomatic. Thyroid scan shows low iodine uptake.

Postpartum thyroiditis tends to recur after subsequent pregnancies, hence may ultimately lead to permanent hypothyroidism. No treatment is needed except betablockers during early period of hyperthyroidism.

**310. What are the complications of hyperthyroidism?**

**Ans.** They are:

1. Precipitation of angina in a patient with IHD and CHF and digitalis toxicity in patients with valvular heart disease receiving digitalis.
2. Cardiac arrhythmias (atrial fibrillation is commonest)
3. Thyrotoxic myopathy (proximal muscle weakness)
4. Thyrotoxic hypokalaemic periodic paralysis
5. Thyrotoxic crisis/thyroid storm
6. Malabsorption syndrome.

**311. What are the eye signs of thyrotoxicosis?**

**Ans.** The various eye signs are:

*Von Graefe's:* Upper lid lag

*Joffroy's:* Absence of wrinkling on forehead when asked to look upwards with face inclined downward.

*Gilford's:* Non-retraction of upper lid manually.

*Lochlur's:* Stare look.

*Naffziger's:* Protrusion from super ciliary phase

*Dalrymple's:* Visible upper sclera.

*Moebius:* Failure to converge eyeballs.

*Stellwags':* Stare look, infrequent blinking, widening of palpebral fissure.

N.B.: Read the signs and their method of demonstration in clinical methods in medicine by Dr SN Chugh.

**CASE 25: HYPOTHYROIDISM**

The young girl (12 yr) (Fig. 1.25A) presented with puffiness of face, weight gain, hoarseness of voice, protuberent abdomen, laziness, and lethargy. She has dropped schooling at the age of 10. She has delayed milestones and has mental insufficiency according to the parents. The another patient 35 yr F (Fig. 1.25B) presented with recent weight gain, constipation, cold intolerance and puffiness of face with hoarseness of voice.

Examination revealed mental insufficiency (IQ 50%) in patient Fig. 1.25A, otherwise both the patients have coarse facial features, thick lips, puffiness of face, thick dry rough skin, bradycardia, hoarseness and nonpitting pedal oedema. The patient Fig. 1.25B has hypertension (BP 150/100 mmHg).



**Figs 1.25A and B: Hypothyroidism.** A. Cretinism (infantile onset of hypothyroidism); B. Adult hypothyroidism

**Points to be noted in history**

- Onset of symptoms and their progression
- History of recent weight gain, change in appearance, malaise and tiredness and slowness of activity
- History of cold intolerance, change in mood or behavior disturbance, deafness
- History of arthralgia, myalgia, dryness of skin, decreased sweating
- History of menstrual irregularity, poor libido, sterility
- History of anorexia, constipation
- History of delayed milestones, slow mentation or mental insufficiency in a child

**General Physical Examination (GPE)**

- **Face.** Note puffiness or periorbital oedema, coarse thick facial appearance, rounded face
- **Eyes** for xanthelasma
- **Tongue** Large protruding (macroglossia)
- **Lips** thick
- **Neck** examination for JVP, thyroid enlargement and lymph node
- **Pulse, BP, temp.** and respiration
- **Skin** Note the texture, dryness, coarse (toad-like)
- **Hair** The hair are sparse, thin, brittle in hypothyroidism
- **Hands** Dry cold hands, thick skin, creases of palm prominent
- **Feet** Note dryness and nonpitting oedema

**Systemic Examination**

- CVS examination
  - Examine the heart for evidence of CHF and pericardial effusion
- Examination of abdomen
  - For adynamic ileus and any organ enlargement
- Nervous system
  - Higher function for mental insufficiency
  - VIII nerve exam for deafness
  - Motor system for myopathy (proximal), myotonia and for delayed reflexes
  - Sensory system for peripheral neuropathy, carpal tunnel syndrome
- Respiratory system
  - Chest wall is thick with decreased and slow movements

**Clinical Presentations**

- Infants (<1 year) present with mental retardation, pot belly, large protruding tongue (macroglossia), flat nose, dry skin, sparse hair and delayed milestones of development. Other features of hypothyroidism are present. The condition is called *Cretinism*. This may persist in childhood.
- The adolescents with hypothyroidism (juvenile hypothyroidism) present with short stature, retarded growth, poor performance at school, delayed puberty and sexual maturation. Other features of adult hypothyroidism are present.
- The adult patients present usually with myxedema in which features of hypothyroidism are associated with myxomatous changes in skin (dry, toad-like skin, puffiness of face, hands and feet), larynx (hoarseness of voice or slurred speech), and ear (leading to deafness). They may complain of carpal tunnel syndrome (entrapment neuropathy).
- Majority of the women with mild hypothyroidism present with increase in weight, menstrual irregularity, mental feature (depression) or slowness of activity and generalised ache and pains.

**Table 1.75:** Symptoms and signs of adult hypothyroidism

<b>General features</b>	Tiredness, weight gain, cold intolerance, hoarseness of voice and lethargy are common. Somnolence and goitre are less common. Non-pitting oedema over feet and legs common. "Peaches and cream" complexion may occur
<b>Cardiovascular</b>	Slow pulse rate or bradycardia, hypertension and xanthelasma are common Pericardial effusion, precipitation of angina and cardiac failure less common
<b>Neuromuscular</b>	Aches and pains, delayed relaxation of ankle jerks, muscle stiffness are common Carpal tunnel syndrome, deafness, psychosis, depression, myotonia and proximal myopathy are less common
<b>Haematological</b>	Anaemia may be present
<b>Dermatological</b>	Dry thick skin (toad skin), sparse hair including loss of hair on lateral third of eyebrow, nonpitting oedema are common. Hypothermia is common. Vitiligo and alopecia are rare
<b>Reproductive</b>	Menorrhagia, infertility (common), galactorrhoea and impotence (less common)
<b>Gastrointestinal</b>	Constipation (common) and adynamic ileus (less common)

**312. What is your clinical diagnosis:**

**Ans.** The patient 1 (12F) has features suggestive of hypothyroidism (cretinism). Read the features in next question. The patient 2, adult female has all features suggestive of myxoedema (adult-hypothyroidism).

**313. What are the clinical features of hypothyroidism in these cases?**

**Ans.** The clinical features of hypothyroidism are tabulated (Table 1.75).

**314. What is hypothyroidism?**

**Ans.** Hypothyroidism is a clinical condition reflecting hypofunctioning of thyroid gland, characterised by low levels of circulating thyroid hormones. It is called *primary* when the cause of it lies in the thyroid gland itself. It becomes *secondary* when hypothyroidism occurs due to disease of anterior pituitary or hypothalamus.

*Goitrous hypothyroidism* means enlargement of thyroid gland associated with hypothyroidism.

*Subclinical hypothyroidism* means biochemical evidence of hypothyroidism (low to normal T3 and T4 but raised TSH) without any symptoms of hypothyroidism (asymptomatic hypothyroidism). The cause of subclinical hypothyroidism are same as described under transient hypothyroidism. It may persist for many years. Treatment with replacement therapy with small dose of thyroxine is indicated.

*Transient hypothyroidism* refers to a state of reversible thyroid function, often observed during the first 6 months of:

1. Subtotal thyroidectomy or  $^{131}\text{I}$  treatment of Graves' disease
2. Post-thyrotoxic phase of subacute thyroiditis
3. Postpartum thyroiditis
4. In some neonates, transplacental passage of TSH receptors- binding antibodies (TRABs) from the mother with Graves' disease or autoimmune thyroid disease may cause transient hypothyroidism.

*Congenital hypothyroidism* is asymptomatic state detected during routine screening of TSH levels in spot blood samples obtained 5-7 days after birth. It results either from thyroid agenesis, ectopic hypoplastic glands or from dysmorphogenesis. Early detection and early treatment with replacement thyroxine therapy is mandatory to prevent irreversible brain damage.

**315. What are the causes of hypothyroidism?**

**Ans.** These are:

1. *Spontaneous atrophic or idiopathic hypothyroidism*
2. *Goitrous hypothyroidism*
  - Hashimoto's thyroiditis
  - Iodine deficiency
  - Drug-induced (PAS, phenylbutazone, lithium, iodides)
  - Dysmorphogenesis
3. *Postablative*
  - Following surgery
  - Following  $^{131}\text{I}$
4. *Transient during thyroiditis*
  - Subacute
  - Postpartum



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5. *Maternally transmitted* (iodides, antithyroid drugs, TRABs antibodies)

### 316. What is Hashimoto's thyroiditis?

**Ans.** It is an autoimmune thyroiditis characterised by:

- A common cause of goitrous hypothyroidism
- More common in females in age group of 20-50 years
- Goitre is diffuse, firm or rubbery in consistency
- 25% of patients presents with hypothyroidism at the onset, while others develop it subsequently.
- Majority of the patients (90%) have thyroid peroxidase antibodies present in the serum.
- Small doses of thyroxine (50 µg) are needed to overcome hypothyroidism as well as to suppress TSH.

### 317. What is Pendred's syndrome?

**Ans.** It is a genetically determined syndrome (autosomal inheritance) consisting of a combination of dysmorphogenetic goitre and nerve deafness. The dysmorphogenesis is due to deficiency of intrathyroidal peroxidase enzyme.

### 318. What is the relation between iodine and hypothyroidism?

**Ans.** Both iodine deficiency and iodine excess can produce hypothyroidism.

Iodine when taken for prolonged period (iodine excess) in the form of expectorants containing potassium iodide or use of amiodarone (contains a significant amount of iodine) may cause goitrous hypothyroidism by inhibiting the release of thyroid hormones. This is common in patients with underlying autoimmune thyroiditis.

Iodine deficiency in certain parts of the world especially Himalayas, produces endemic goitre (>70% of the population is affected). Most of the patients usually are euthyroid and have normal or raised TSH levels. In general, more severe is the iodine deficiency, the greater is the incidence of hypothyroidism.

### 319. How will you diagnose hypothyroidism?

**Ans.** The diagnosis is made on the basis of:

1. Clinical manifestations
2. Investigations

The investigations are done to confirm the diagnosis, to differentiate between primary and secondary hypothy-

**Table 1.76:** Thyroid hormone levels in various forms of hypothyroidism

Hormone	Primary	Secondary	Subclinical
T3	Low	Low	Normal (lower limit of normal)
T4	Low	Low	Normal (lower limit of normal)
TSH	High	Low	Slightly high

roidism, for follow-up of treatment and to monitor the response. The TSH levels are used to monitor the response to treatment (Table 1.76).

#### Other Tests

- Serum cholesterol is high
- ECG may show bradycardia, low voltage graph and ST-T changes
- Blood examination may reveal anaemia (usually normocytic or macrocytic)
- Thyroid peroxidase antibodies (TPO) help to find out the cause of hypothyroidism. Their presence indicate autoimmune thyroiditis as the cause of hypothyroidism.
- *X-ray chest.* It may be normal or may show cardiomegaly due to pericardial effusion – common in primary rather than secondary hypothyroidism.
- Photomotogram – recording of ankle jerk shows slow-contraction and delayed relaxation.

### 320. How does simple goitre differ from goitrous hypothyroidism?

**Ans.** The difference between simple diffuse goitre and Hashimoto's thyroiditis are given in Table 1.77.

### 321. What are the complications of myxedema?

**Ans.** Complications arise as a result of infiltration of myxomatous tissue in various other structures, especially in primary myxedema.

1. CVS, e.g. pericardial effusion, restrictive cardiomyopathy, conduction disturbances
2. Respiratory. Cor pulmonale, type 2 respiratory failure
3. Myxedematous madness and myxedema coma
4. Entrapment neuropathy (Carpal-Tunnel syndrome).



**Table 1.77:** Differentiation between two common diffuse goitre

<i>Features</i>	<i>Simple diffuse goitre</i>	<i>Goitre due to Hashimoto thyroiditis</i>
Age	Common in young girls (15-25 years) or during pregnancy	Common in young females (20-50 years)
Thyroid enlargement	Mild, tends to be noticed by friends and relatives	Large, visible from distance
Goitre	Soft, nontender	Firm, tender
Prevalence	Endemic or sporadic	Sporadic
Symptoms	Asymptomatic or there is a tight sensation in neck Patient seeks medical attention from asthetic point of view	Pain radiating to jaw or neck, increased during swallowing, coughing and neck movements
Cause	Suboptimal dietary iodine intake and minor degrees of dyshormogenesis	Autoimmune disease, may be associated with other autoimmune conditions
Thyroid status	Normal	25% cases are hypothyroid at presentation, others become later on. Initially, there may be transient thyrotoxicosis
Thyroid antibodies (TPO antibodies)	Negative	Positive (95% cases)

**CASE 26: DIABETESE MELLITUS**

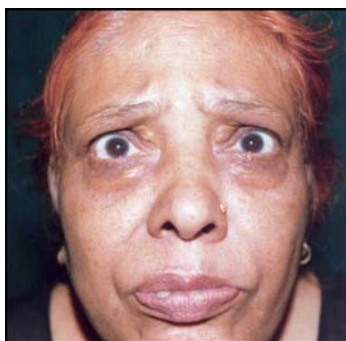
- I. 18 years male (Fig. 1.26A) presented with diabetic ketoacidosis as an emergency. On recovery he gave history of polyuria, polydipsia, polyphagia and weakness.
- II. A 45 years female (Fig. 1.26B) presented with history of polyuria, polydipsia and puffiness of face and oedema feet. She admitted a past history of diabetes for the last 5 yrs taking antidiabetic medication.

**Points to be noted in history**

- Onset of symptoms and their course
- Ask any history of fever, cough, expectoration, haemoptysis, pain chest, night sweats, fatigue, etc.
- Ask for history of dysuria, pyuria, increased frequency, burning micturition
- History of chronic diarrhoea, vomiting, gastric distension
- History of breathlessness, orthopnoea, PND, etc.
- Ask for oedema feet or legs
- History of menstrual irregularity, sterility, vaginal discharge etc.
- History of paraesthesias, loss of sensations, motor deficit (monoplegia, paraplegia, etc), facial asymmetry deafness, mental features, disturbance in consciousness
- Ask for symptoms of hypoglycaemia such as profuse sweating, palpitation, air hunger, nausea and convulsions, etc.
- History of visual disturbance or visual loss or decreased vision.

**General Physical Examination**

- Body habitus/fat distribution
- Dry mouth/dehydration (dry tongue)
- Air hunger
- Skin and mucosal sepsis, candidiasis
- Skin pigmentation, vitiligo, dermopathy
- Weight loss (insulin deficiency)
- Obesity-may be abdominal (insulin resistance)
- White spots on shoes (glycosuria)
- Deep sighing respiration (Kussmaul breathing)
- Eyes for xanthelasma, evidence of infection
- Ear for infection and deafness

**Fig. 1.26A: Type 1 diabetes****Fig. 1.26B: Type 2 diabetes****Clinical Presentations**

1. Asymptomatic diabetes. The diabetes is detected on investigations.
2. Type 1 diabetics (acute presentation)
  - Type I diabetics present with a symptom triad of polyuria, polydipsia and polyphagia along with weakness and marked weight loss.
3. Subacute presentation: The clinical onset may be over several months; occurs commonly in older patients who complain of thirst, polyuria, weight loss, lack of energy, visual disturbance, changes in eye-refraction and pruritus vulvae (in females).
4. Type 1 diabetics may also present with complications such as ketoacidosis, diabetic neuropathy and/or nephropathy.
5. Type 2 diabetics present in different speciality with different complaints (Table 1.78).

**Systemic Examination****I. Nervous System**

- Test higher mental functions.
- Cranial nerve examination.

**Visual acuity**

- Distance vision using Snellen chart at 6 metres
- Near vision using standard reading chart
- Impaired visual acuity may indicate the presence of diabetic eye disease, and serial decline may suggest development or progression in severity.

**Lens opacification**

- Look for the red reflex using the ophthalmoscope held 30 cm from the eye
- The presence of lens opacities or cataract should be noted.

**Fundus examination**

- The pupils must be dilated with a mydriatic (e.g. tropicamide) and examined in a dark clear room.
- Features of diabetic retinopathy should be noted including evidence of previous laser treatment which leaves photo-coagulation scars.

**Sensations; test the followings;**

- Light touch.
- Vibration sense: use of 128 Hz tuning fork over big toe/malleoli
- Pin-prick: use pin.
- Pain: pressure over Achilles tendon, calf tenderness on squeezing
- Proprioception: test position sense at big toe
- Test for distal anaesthesia/ hypo-aesthesia in glove- stocking distribution

**Reflexes**

- Test plantar and ankle reflexes.

**II. Cardiovascular System**

- Pulses. Palpate all the peripheral pulses. Capillary refill should be tested
- Examine the heart for cardiomegaly. Auscultate the heart for any murmur or rub or an abnormal sound

**III. Respiratory System**

- Examine for any evidence of tuberculosis, pneumonia, pleural effusion or empyema

- Neck examination for JVP, lymph nodes enlargement and carotid pulsations
- Record pulse, BP, temperature and respiration.

#### *Insulin injection sites*

Main areas used and the abnormalities thereof

- Anterior abdominal wall
- Upper thighs/buttocks
- Upper outer arms
- Lumps (lipodystrophy)
- Subcutaneous fat deposition (lipohypertrophy)
- Subcutaneous fat loss (lipoatrophy; associated with injection of unpurified animal insulins—now rare)
- Erythema, infection (rare)

#### **Examination of the Hands**

- Limited joint mobility (sometimes called ‘cheiroarthropathy’) may be present, this is the inability to extend (5 to 180°) the metacarpophalangeal or interphalangeal joints of at least one finger bilaterally. The effect can be demonstrated in the prayer sign. causes painless stiffness in the hands, and it occasionally affects the wrists and shoulders.
- Dupuytren’s contracture is common in diabetes and may include nodules or thickening of the skin and knuckle pads
- Carpal tunnel syndrome is common in diabetes and presents with wrist pain radiating to the hand
- Trigger finger (flexor tenosynovitis) may be present in people with diabetes
- Muscle-wasting /sensory changes may be present as features of a peripheral sensorimotor neuropathy, although this is more common in the lower limbs.

#### **Examination of the Feet**

- Look for evidence of callus formation on weight-bearing areas, clawing of the toes (a feature of neuropathy), loss of the plantar arch, discolouration of the skin (ischemia), localised infection and the presence of ulcers.
- Deformity of the feet may be present, especially in Charcot neuroarthropathy.
- Fungal infection may affect skin between toes, and nails.

#### **Examination of Legs**

- Muscle wasting, sensory abnormality
- Granuloma annulare
- Hair loss
- Tendon reflexes lost

#### *IV. Examination of Abdomen*

- Palpate for liver, spleen or kidney enlargement
- Palpate for any other mass

#### *V. Genitourinary System*

- Examine the penis for evidence of infection or discharge per urethra. Examine scrotum and epididymus for tenderness or swelling
- Examine vulva and vagina for evidence of infection and discharge. Perform per vaginal examination also.

**322. How do you define diabetes mellitus and impaired glucose tolerance (IGT)?**

**Ans.** A clinical syndrome of hyperglycaemia with or without glycosuria either due to lack of insulin (type 1) or insufficiency of insulin with insulin resistance (type 2) is termed diabetes mellitus.

*Impaired glucose tolerance (IGT):* is defined as an abnormal response to 75 g of oral glucose on glucose tolerance test. Fasting blood sugar < 126 mg and postprandial glucose between 180 to 200 mg indicate IGT.

**323. What is gestational diabetes mellitus (GDM)?**

**Ans.** Glucose tolerance is impaired during pregnancy, results as a result of insulin resistance related to metabolic changes of late pregnancy, increases insulin requirement and may lead to impaired glucose tolerance and GDM. GDM occurs in about 4% women during pregnancy which reverts to normal glucose tolerance in postpartum, but there is risk of developing permanent DM later in life.

**324. What are the clinical presentations of type 2 diabetes?**

**Ans.** See the Table 1.78.

**325. How do you classify diabetes?**

**Ans.** Diabetes mellitus (DM) has been classified on the basis of pathogenic process as opposed to earlier criteria of age of onset and type of therapy. The broad categories of DM are type 1 and type 2. Type 1 is divided into A and B. A means immunological destruction of pancreas leading to insulin deficiency (autoimmune type) while B is nonautoimmune idiopathic (Table 1.79). Type 2 DM is a heterogeneous group of disorders characterised by variable degree of insulin resistance, impaired glucose secretion and increased glucose production. Type 2 DM is preceded by a period of abnormal glucose homeostasis classified as impaired fasting glycaemia or impaired glucose tolerance.

**326. What is pathogenesis of type 1 diabetes?**

**Ans.** It is considered as an autoimmune disorder. The various criteria of autoimmunity are given in the Box 1.1. Genetic susceptibility is a major determinant while environmental factors act as a trigger to initiate autoimmune destruction of beta cells of the pancreas.

**Table 1.78:** Clinical presentation of type 2 DM (NIDDM)

These patients present to different specialties or superspecialties with following features which arise as a result of complications. The organs/systems involvement and their presenting features are as follows:

Organ/system affected	Clinical presentation
• <b>Eye</b>	• Recurrent styes, chalazion, anterior uveitis (hypopyon), frequent change of glasses due to error of refraction, visual impairment due to premature development of cataract or retinopathy
• <b>Urinary tract</b>	• Urinary tract infections, acute pyelitis or pyelonephritis, nephrotic syndrome
• <b>GI tract</b>	• Chronic diarrhoea, malabsorption, gastroparesis (dilatation of stomach)
• <b>Genital tract</b>	• Females present with pruritus vulvae, vaginal discharge, menstrual irregularities, recurrent abortions, infertility, etc.
• <b>Cardiovascular</b>	• Ischemic heart disease, hypertension, peripheral vascular disease (cold extremities, absent peripheral pulses, gangrene or diabetic foot)
• <b>Nervous</b>	• Peripheral neuritis (tingling sensations in the extremities with numbness) symptoms of autonomic neuropathy (Table 1.93), cerebral ischemic episodes and strokes.
• <b>Skin</b>	• Multiple boils, carbuncles, abscesses, non-healing wounds, mucocutaneous candidiasis
• <b>Respiratory</b>	• Pneumonias, lung abscess, tuberculosis, etc.

The genetic predisposition is HLA linked class II genes at D locus (DR<sub>3</sub> and D<sub>4</sub>) on short arm of chromosome 6. Immunological response results in production of class II beta cell specific molecules which play a role in autoimmune destruction. Beta cell mass declines, insulin secretion becomes progressively impaired although normal glucose tolerance is maintained. The rate of decline of beta-cell mass varies with some patients progressing rapidly to clinical diabetes, while others evolving slowly. Features of diabetes will appear once > 80% of beta cells have been destroyed. At this point, residual functional existing beta cells are insufficient in number to maintain glucose tolerance. Thus, there is a transition period between impaired glucose tolerance with increase in requirement of insulin to frank diabetes. After the onset of type 1A diabetes, there is “honeymoon”

**Table 1.79:** Classification of DM based on aetiology

<b>I. Type 1 diabetes mellitus</b> (beta-cell destruction with absolute insulin deficiency)
A. Immune-mediated
B. Unknown mechanism (idiopathic)
<b>II. Type 2 DM</b> (either due to insulin resistance with relative insulin deficiency or insulin secretion defect with insulin resistance)
<b>III. Other specific types of diabetes</b>
A. Genetic defect of beta-cell function leading to gene mutation) <ul style="list-style-type: none"> <li>• MODY 1 (hepatocyte nuclear transcription factor (HNF-4-alpha)</li> <li>• MODY 2 (Glucokinase). MODY3 (HNF-1-alpha)</li> <li>• MODY4 (insulin promotor factor, MODY5 (HNF-1-beta), MODY 6(Neuro DI)</li> <li>• Proinsulin or insulin conversion</li> </ul>
B. Genetic defect in insulin action <ul style="list-style-type: none"> <li>• Type I insulin resistant.</li> <li>• Lipodystrophy syndromes</li> </ul>
C. Pancreatic diabetes (pancreatitis, hemochromatosis, cystic fibrosis)
D. Endocrinopathies (acromegaly, Cushing's syndrome, thyrotoxicosis, pheochromocytoma)
E. Drug and chemical induced
F. Other genetic syndromes, e.g. Down's and Klinefelter's syndrome, DIDMOAD (diabetes insipidus, DM, optic atrophy and deafness) Turner's syndrome, hereditary ataxia, Huntington's chorea, Laurence-Moon-Biedl and dystrophic myotonia
<b>IV. Gestational diabetes mellitus (GDM)</b>

period of 1 to 2 years during which glycaemic control is achieved with modest dose of insulin or rarely, insulin is not required. This is a transient or fleeting phase of endogenous insulin production from beta cells, which subsequently disappears as the autoimmune process progresses and ultimately individual becomes completely insulin deficient.

**Box 1.1:** Points in favour of autoimmunity

- HLA linkage
- Its association with other autoimmune disorders
- Lymphocytic infiltration of beta cells pancreas
- Circulating anti-insulin antibodies
- Recurrence of beta cells destruction in pancreas

**327. What is pathogenesis of clinical features of type 1 diabetes and ketoacidosis?**

**Ans.** Lack of insulin stimulates counter-regulatory hormone release, e.g. glucagon, GH and catecholamines

**Table 1.80:** General clinical characteristics of type 1 and type 2 DM

Features	IDDM (Type 1) (Fig. 1.26A)	NIDDM (Type 2) (Fig. 1.26B)
1. Gene locus	Chromosome 6	Chromosome 11
2. Age of onset	< 30 years	> 30 years
3. Onset of symptoms	Rapid	Slow
4. Body weight	Thin, lean	Normal weight or obese
5. Duration of symptoms	Weeks	Months or years
6. Presenting features	Polyuria, polydipsia, polyphagia	Present with different complications
7. Ketonuria	Present (Ketone-prone)	Absent (Ketone-resistant)
8. Complications at the time of diagnosis	Absent	Present (10-20%)
9. Family history	Negative	Positive
10. Plasma insulin	Low or absent	Normal to high
11. Choice of treatment	Insulin	Oral hypoglycemics
12. Mortality if untreated	High	Low

in addition to stimulation of catabolism of nutrients producing neoglucogenesis, glycogenolysis and liposis and subsequently ketoacidosis. Lack of insulin results in hyperglycaemia due to increased hepatic output of glucose and poor peripheral utilisation of glucose. Glycosuria, osmotic diuresis and salt and water loss are its consequences which produce various clinical features of type I diabetes. Diabetic ketoacidosis is an acute metabolic complication, requires urgent diagnosis and management.

**328. What are the differences between type 1 and type 2 DM?**

**Ans.** Table 1.80 deals with general clinical characteristics of type 1 and type 2 DM.

**329. How do you diagnose DM?**

**Ans.** Table 1.81 describes criteria for diagnosing diabetes mellitus and other related complications.

**330. What is hyperosmolar Nonketotic Diabetic Coma? How does it differ from diabetic ketotic coma?**

**Ans.** It is common in elderly people with type 2 diabetes with several weeks history of polyuria, weight loss and diminished oral intake followed by confusion and coma.



**Table 1.81:** American Diabetic Association (1997) criteria endorsed by WHO (1998) for diagnosis of diabetes or other related conditions

Condition	Venous plasma glucose concentration in mg% (mmol/L)	
	Fasting	Postprandial (2 hr GTT)
Normal	<110 (6.1)	<140 (7.3)
Diabetes	>126	>200
<b>Or</b>		
Symptoms of diabetes plus random blood sugar $\geq$ 200 mg% (11.1 mmol/l)		
Impaired fasting glycaemia	110-126 (6.1-7.0)	<140 (7.8)
Impaired glucose tolerance	<126 (7.0)	$\geq$ 140 but <200 (7.8-11.1)

*Note:* 2 hours GTT means following 75 g glucose load. Venous blood glucose concentration is lower than capillary blood. Whole blood glucose is lower than plasma because RBC contain little glucose.

The physical examination reveals marked dehydration, hypotension, tachycardia and altered mental status. The GI symptoms and Kussmaul acidotic breathing are notably absent. The precipitating factors are:

- Any concurrent illness, infection, sepsis
- Acute event such as MI, stroke
- Following procedures such as- haemodialysis

**The biochemical characteristics** of this coma include:

- Hyperglycaemia (blood glucose >600 mg%)
- Hyperosmolality (>350 mOsm/l). Normal osmolality 280-290 mOsm/l.
- Absent or minimal ketone body in the blood or urine. The marked dehydration and relative deficiency of insulin are presumed to be factors for absence of ketosis in this coma. Acidosis is also absent.
- Pre-renal azotemia

The two common types of coma in type 2 diabetes are compared in Table 1.82.

### 331. Name the various types of coma in DM.

**Ans.** These are:

1. Diabetic ketotic coma
2. Hyperosmolar hyperglycaemic, nonketotic coma
3. Hypoglycaemic coma
4. Lactic acidosis coma.

### 332. What are chronic or late complications of DM?

**Ans.** Chronic complications can be divided into vascular and nonvascular (Table 1.83); the vascular are

**Table 1.82:** Differentiating features between two types of coma in diabetics

Feature	Hyperosmolar non-ketotic coma	Diabetic ketotic coma
Occurrence	Type 2 diabetes	Type I diabetes
Precipitating factors	Procedure, drugs, documented infection. MI, stroke	Too much food with no or little insulin or infection
Blood glucose	Usually >600 mg%	Usually <600 mg%
Osmolality	Markedly increased (>350 mOsm/l)	Slightly increased
Ketosis	Absent or minimal	Present
Acidosis (Kussmaul breathing)	Absent	Present
Insulin	Small dose required	Large dose required
Fluids	Half normal saline (0.45% NaCl)	Normal saline
Mortality	Not high	Very high

further divided into microvascular and macrovascular. Since type 2 DM has a long asymptomatic period of hyperglycaemia, many individuals with type 2 DM have complications at the time of diagnosis.

### 333. What are pathogenic mechanisms for complications of DM?

**Ans.** The pathogenic mechanisms are:

- Activation of polyol pathway
- Formation of advanced glycation end products (AGEs) leading to endothelial dysfunction

**Table 1.83:** Chronic or long-term complications of DM

<b>I. Vascular</b>
<b>A. Microvascular</b>
i. Eye disease
• Retinopathy (see Table 1.85)
• Macular edema
ii. Neuropathy, e.g. sensory, motor, mixed, autonomic (see Table 1.84)
iii. Nephropathy
<b>B. Macrovascular</b>
• Coronary artery disease
• Peripheral vascular disease
• Cerebrovascular disease
• Diabetic foot
• Hypertension
<b>II. Others/nonvascular</b>
• Gastrointestinal, e.g. gastroparesis, diarrhoea
• Genitourinary (nephropathy (Fig. 1.26E)/sexual dysfunction)
• Dermatologic
• Infections/pressure sore (Fig. 1.26D)
• Cataracts
• Glaucoma

- Activation of protein kinase-C-second messenger system
- Oxidative stress

All these mechanisms lead to endothelial dysfunction and development of vascular complications.

**334. What are various neurological complications in DM? How do you manage them?**

**Ans.** These may be somatic or autonomic (Table 1.84).

**335. What are the autonomic disturbances in diabetes?**

**Ans.** Read the Table 1.84.

**336. What is glycosylated haemoglobin? What is its significance?**

**Ans.** The haemoglobin (Hb) gets glycosylated due to formation of a covalent bond between glucose molecule and  $\beta$ -chain of haemoglobin. Glycosylated Hb is related to prevailing glucose concentration, hence, hyperglycaemia and its excursions lead to increased glycosylation. Glycosylated Hb is expressed as percentage of normal haemoglobin (4-8% depending on the technique of measurement).

It is parameter of long-term control (i.e. past 6 weeks) of DM because its is an index of average blood glucose concentration over the life of the hemoglobin molecule (e.g. approx 6 weeks). Its higher values reflect various grades of control of DM. The target value of glycosylated Hb (HbA1c) for control of diabetes is < 7% so as to retard or delay the onset of complications.

**337. What is diabetic retinopathy? What are ocular fundi changes in DM?**

**Ans.** The involvement of retina (basement membrane, blood vessels) in diabetes is called *diabetic retinopathy*. It is an important cause of blindness among diabetics. Early detection and early management are essential. Ocular fundi should be checked regularly to detect asymptomatic disease. The fundoscopic findings are given in Table 1.85.

The dot (microaneurysms) and blot (leakage of blood into deeper layer) haemorrhages are the earliest and characteristic findings of background retinopathy in DM.

**338. What are the clinical stages and time course of diabetic nephropathy?**

**Ans.** The clinical stages and their time course is as follows:

1. *Stage of microalbuminuria* (incipient nephropathy). It takes 5 years for its appearance
2. *Overt proteinuria* (non-nephrotic range). They take 5-10 years for development
3. *Nephrotic syndrome* (Fig. 1.26). It takes 5-10 years for development
4. *Renal failure/insufficiency* | Both these stages take
5. *End stage renal disease (ESRD)* | 10-15 years for their development

**339. Why dose of insulin decreases in diabetic nephropathy?**

**Ans.** It is due to:

- Excretion of insulin binding antibodies with albumin in urine
- Decreased degradation of insulin
- CRF tends to impair neoglucogenesis

**Table 1.84:** Classification, clinical features and steps of management of diabetic neuropathy

Classification	Symptoms and signs	Treatment
<b>1. Somatic</b>		
<b>a. Symmetric sensory and distal</b>	<ul style="list-style-type: none"> <li>• Tingling or burning sensation in the extremities (hands and feet), nocturnal pain in limbs, numbness and coldness of extremities.</li> <li>• Glove and stocking type of anaesthesia</li> <li>• Loss of tendon reflexes and muscle wasting</li> <li>• Disorganisation of joints (Charcot's joints)</li> <li>• Abnormal gait (wide based, thumping gait)</li> <li>• Nerve conduction velocity delayed in distal parts</li> </ul>	<ul style="list-style-type: none"> <li>• To maintain near or near normal metabolic control on long-term basis with insulin</li> <li>• Insulin is better for control than OHA</li> <li>• Symptomatic relief of pain in extremities is achieved by anti-depressants (imipramine or amitriptyline) or by anti-epileptics (dilatant or carbamazepine or gabapentine or valproate)</li> </ul>
<b>b. Asymmetric, motor, proximal (diabetic amyotrophy)</b>	<ul style="list-style-type: none"> <li>• Lower motor neuron paralysis with wasting of muscles</li> <li>• Hyper or hypoesthesia may be present on anterior aspect of thighs.</li> <li>• Lower limbs are commonly involved than upper limbs.</li> <li>• Tendon reflexes are lost on affected side</li> <li>• Lumbosacral area is site of involvement</li> </ul>	<ul style="list-style-type: none"> <li>• Aldolase reductase inhibitors may be useful, if available.</li> <li>• Optimal control will not only delay the progress of neuropathy but metabolic complications may even be reversed</li> </ul>
<b>Mononeuropathy</b>		
<ul style="list-style-type: none"> <li>• Mononeuritis (cranial or spinal)</li> <li>• Mononeuritis multiplex</li> </ul>	<ul style="list-style-type: none"> <li>• 3rd and 6th cranial nerves involvement common producing diplopia and loss of eye movements</li> <li>• Carpal tunnel syndrome with ulnar and median nerve involvement (wrist drop)</li> <li>• Foot drop; due to sciatic or popliteal nerve involvement</li> </ul>	
<b>2. Autonomic (visceral)</b>		
<b>a. Cardiovascular</b>	<ul style="list-style-type: none"> <li>• Vertigo, giddiness and blurring of vision due to postural hypotension, resting tachycardia and fixed heart rate</li> </ul>	<ul style="list-style-type: none"> <li>• Support the limbs by stockings</li> <li>• Fludrocortisone therapy to raise BP</li> <li>• Monitor Na<sup>+</sup>, K<sup>+</sup> and BP</li> </ul>
<b>b. Gastrointestinal</b>	<ul style="list-style-type: none"> <li>• Nausea, vomiting, abdominal distension, nocturnal diarrhoea, constipation due to colonic atony, gastroparesis, dysphagia due to oesophageal atony</li> </ul>	<ul style="list-style-type: none"> <li>• For gastroparesis use metoclopramide</li> <li>• Itopride or mosapride (prokinetic) 5-15 mg/day</li> <li>• For diarrhoea, tetracycline 250 mg after every 6 hours</li> </ul>
<b>c. Genitourinary</b>	Loss of libido, impotence, urinary incontinence, difficulty in micturition (atony of bladder)	<ul style="list-style-type: none"> <li>• Penile prosthesis (silicon rods)</li> <li>• Injection of papaverine into corpora cavernosa</li> </ul>
<b>d. Pseudomotor plus Vasomotor</b>	<ul style="list-style-type: none"> <li>• Abnormal or gustatory sweating, anhidrosis, fissuring of feet, cold extremities, dependent oedema</li> </ul>	<ul style="list-style-type: none"> <li>• Avoid betablockers, methyl dopa, other antihypertensives</li> </ul>
<b>e. Eye (Pupils)</b>	<ul style="list-style-type: none"> <li>• Constriction of pupils, absent or delayed light reflex</li> </ul>	<ul style="list-style-type: none"> <li>• Propantheline 15 mg t.i.d. may relieve gustatory sweating</li> </ul>

**Table 1.85:** Fundoscopic findings in diabetic retinopathy

- Microaneurysms (earlier to appear as dark spots/dots)
- Retinal haemorrhage (blot haemorrhage)
- Hard and soft exudates (cotton wool exudates)
- Neovascularisation (new vessels formation)
- Pre-retinal haemorrhage
- Vitreous haemorrhage
- Retinitis proliferans, fibrosis and retinal detachment

**340. What are GI complications of DM?**

**Ans.** Gastrointestinal complications in DM are:

- Candidiasis or fungal infections of oral cavity (an opportunistic infection)
- Diabetic oesophageal hypomotility and gastroparesis
- Chronic gastritis
- Diabetic enteropathy
- Pancreatitis (chronic) causing steatorrhoea
- Hepatomegaly (fatty infiltration)
- Acalculous cholecystitis.

**341. Name the various microvascular complications of diabetes.**

**Ans.** Read the Table 1.83.

**342. What is microalbuminuria? What is its significance?**

**Ans.** Microalbuminuria is defined as:

- Loss of < 300 mg of albumin in urine over 24 hrs
- Albumin excretion rate in urine is 20 µg/min

It indicates early diabetic nephropathy, a stage from which nephropathy can be reversed with tight metabolic control.

**343. What is diabetic foot?**

**Ans.** Examination of foot is an important part of clinical evaluation of a case with diabetes (Fig. 1.26C).

The clinical features of diabetic foot are given in Table 1.86. Diabetic foot results as a result of neuropathy, vasculopathy and infections.

**344. How will manage a case of type 2 DM?**

**Ans.** The essential steps in the management of type 2 diabetes are represented in the flow chart (Fig. 1.26F).

**345. How will you classify oral hypoglycemics?**

**Ans.** Read Unit V—Drug therapy.

**Fig. 1.26C:** Diabetic foot**Fig. 1.26D:** Pressure sore. The wound is infected (↓)**346. What do you understand by the term insulin sensitizers? Name them. What are their advantages?**

**Ans.** Insulin sensitizers are the drugs which lower the blood sugar in type 2 DM by sensitizing the insulin



**Table 1.86:** Features of diabetic foot

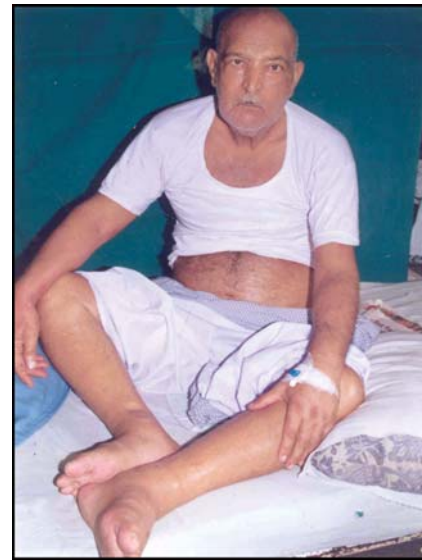
Neuropathy	Vasculopathy
<ul style="list-style-type: none"> <li>• Paraesthesia</li> <li>• Numbness</li> <li>• Pain</li> </ul>	<ul style="list-style-type: none"> <li>• Claudication</li> <li>• Rest pain</li> </ul>
<b>Structural damage</b> <ul style="list-style-type: none"> <li>• Ulcer</li> <li>• Sepsis</li> <li>• Abscess</li> <li>• Osteomyelitis</li> <li>• Digital gangrene</li> <li>• Charcot joint</li> </ul>	

receptors to insulin hence, overcome insulin resistance and hyperinsulinemia in type 2 DM. They are:

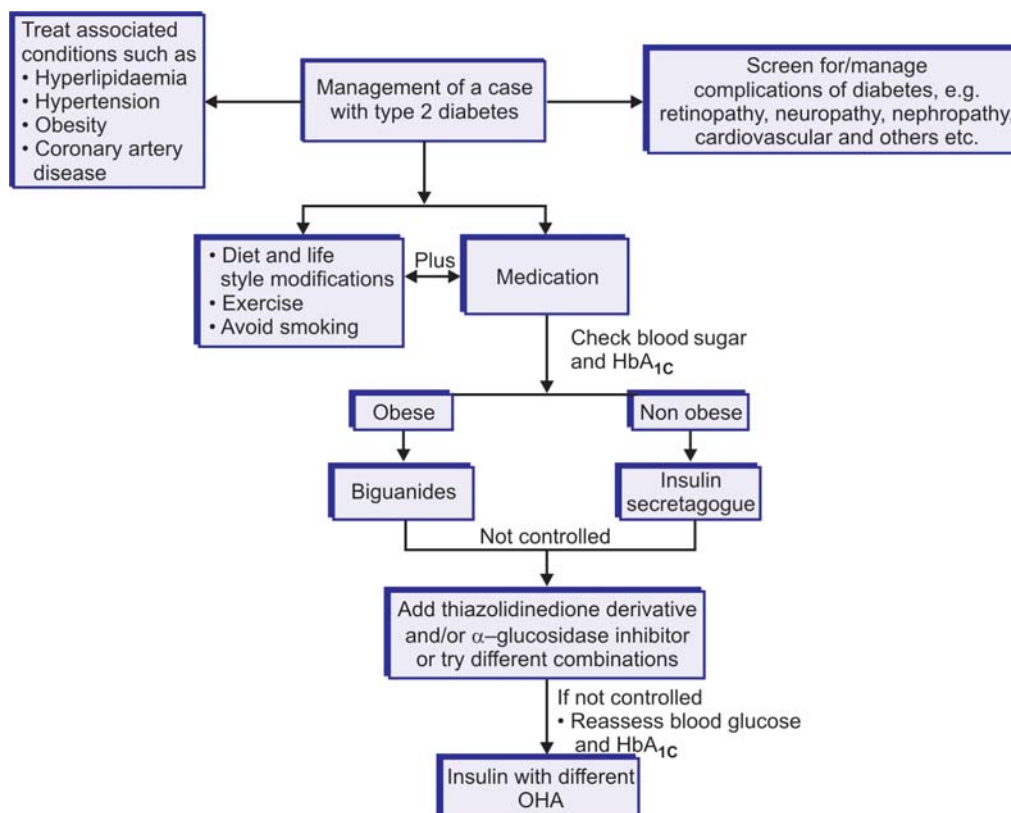
- Biguanides, e.g. *metformin*
- Thiazolidinedione derivatives, e.g. *rosiglitazone*, *proglitazone*.

Advantages are:

- Hypoglycemia is rare as compared to insulin secretagogues, e.g. *sulphonylureas*



**Fig. 1.26E:** Nephrotic syndrome in a patient with diabetes of > 10 years duration. Note the gross oedema and puffiness of face



**Fig. 1.26F:** Management of type 2 diabetic mellitus



- They lower the blood lipid
- They lower the mortality and morbidity
- They can be used to lower blood sugar in patients with impaired glucose tolerance (IGI).

**Warning:** The insulin sensitizers need the presence of insulin for their action, hence, cannot be used in type 1 diabetes mellitus.

### 347. What are key points (Do's and Don'ts) in the management of type 2 DM?

**Ans.** The Do's and Don't's are tabulated (Table 1.87) and illustrated in the Figure 1.26G.

### 348. How will you investigate a case with DM?

**Ans.** The various investigations done are:

#### 1. Blood

- TLC, DLC, ESR for an evidence of infection
- Sugar (fasting and PP) for diagnosis and monitoring of diabetes

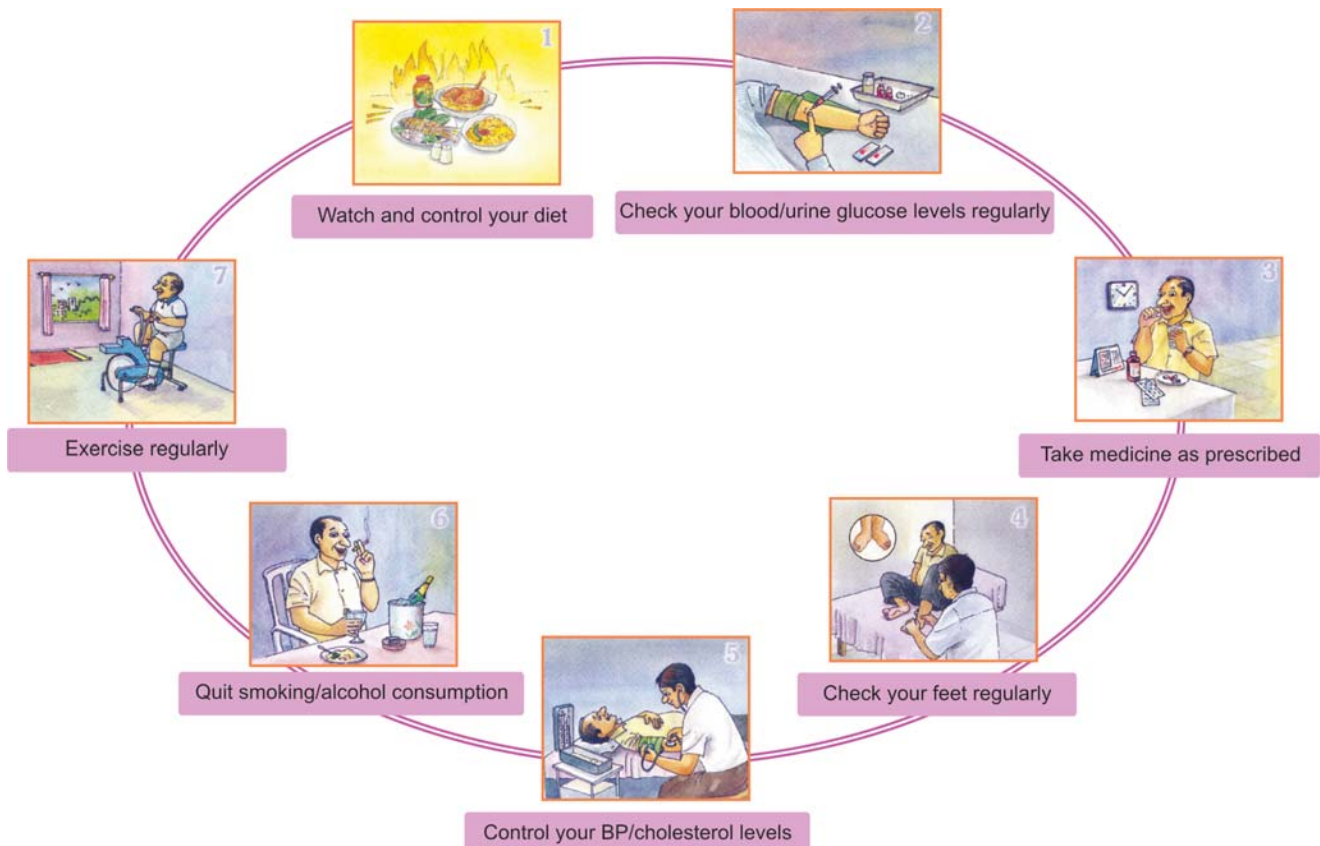
- HbA<sub>1c</sub> (glycosylated Hb) for long-term management of diabetes
- Serum lipids for hyperlipidaemia – a common finding in DM

2. *Urine examination* for specific gravity, pus cells, RBCs, proteins, sugar, casts and culture and sensitivity.
3. *ECG* for diagnosis of silent myocardial infarction or hypertension
4. *Chest X-ray* for pulmonary tuberculosis, fungal infections, cardiomegaly
5. *Fundus examination* for diabetic retinopathy
6. *Other investigations* are specifically performed depending on the system involved.

### 349. What are parameters used for control of DM?

**Ans.** Parameters of control are;

- i. Urine sugar (negative or just positive)
- ii. Blood sugar, e.g.  
F. < 126 mg%      PP < 200 mg%



**Fig. 1.26G:** Key points in the management of type 2 diabetes mellitus

**Table 1.87:** Do's and Don'ts in the management of type 2 DM

	Do's	Don't's
<b>Diet</b>	Eat a balanced diet Eat fibre rich foods  Consume small, frequent meals	Avoid consumption of sweetened beverages, fried foods, alcohol, red-meat, honey, jaggery, sugar, and bakery products Do not skip your meal
<b>Exercise</b>	Exercise should be low to moderate in intensity Consult your doctor before starting any exercise Remember to walk and exercise daily Keep sugar or something sweet, e.g. candy, to avoid low blood sugar levels	Do not exercise if your blood sugar values are low or high and diabetes is not under control Do not exercise on an empty stomach
<b>Foot</b>	Keep your feet clean, warm and dry Change daily clean, soft socks and wear well fitting shoes Examine your shoes daily for cracks, pebbles, nails and other irregularities	Do not use alcohol based solutions. It makes your feet dry. Never walk barefooted Never apply heat of any kind to your feet Do not cut corns or calluses yourself
<b>Eye</b>	Consult your doctor if you have pain in your eyes Have an yearly eye examination done by your doctor	Do not neglect any infection in your eyes.

\*Adapted from 2004 clinical practice recommendations by ADA

iii. Serum lipids

HDL M > 40 mg/dl and F > 60 mg/dl

LDL < 100 mg/dl

Triglycerides < 150 mg/dl

iv. Hb A1c (glycosylated Hb)

- < 6% with a check once in 3 months

### 350. What is hypoglycemia?

**Ans.** It is defined as blood glucose level <45 mg% (2.5 mmol/L). Hypoglycaemia is classified traditionally into (i) postprandial (occurs in response to meals) and (ii) fasting. Fasting hypoglycaemia usually occurs in the presence of disease while postprandial occurs in the absence of a recognisable disease (Table 1.88). The factors responsible for hypoglycaemia are given in Table 1.89.

### 351. What are the symptoms and signs of hypoglycaemia?

**Ans.** Symptoms and signs of hypoglycaemia occur due to effects of low levels of glucose *per se* as well as stimulation of sympathetic system. These are given in Table 1.90.

There is a great degree of variation among individuals in awareness of symptoms of hypoglycaemia in diabetes. Some patients may feel symptoms when blood sugar is

**Table 1.88:** Classification of hypoglycaemia

1. <b>Postprandial hypoglycaemia</b>
<ul style="list-style-type: none"> <li>• Alimentary, e.g. dumping syndrome (following gastric surgery) due to hyperinsulinaemia and idiopathic (true or pseudohypoglycaemia)</li> <li>• Galactosaemia and hereditary fructose intolerance (common causes of hypoglycaemia in children)</li> </ul>
2. <b>Fasting hypoglycaemia</b>
i. Hyperinsulinism
<ul style="list-style-type: none"> <li>• Insulinoma (pancreatic beta-islet cell tumour)</li> <li>• Non-pancreatic tumour secreting insulin- like growth factor I</li> <li>• Excessive exogenous insulin</li> <li>• Drugs, e.g. sulphonylurea, quinine, salicylates, propranolol, pentamidine</li> </ul>
ii. Endocrinal causes
<ul style="list-style-type: none"> <li>• Hypopituitarism. Addison's disease.</li> <li>• Glucagon and catecholamines deficiency</li> </ul>
iii. Liver diseases
<ul style="list-style-type: none"> <li>• Severe hepatitis</li> <li>• Cirrhosis of liver</li> </ul>
iv. Renal disease
<ul style="list-style-type: none"> <li>• Renal failure</li> </ul>
v. Enzymatic defects
<ul style="list-style-type: none"> <li>• G<sub>6</sub> phosphatase</li> <li>• Liver phosphorylase</li> <li>• Pyruvate carboxylase</li> <li>• Glycogen synthetase</li> </ul>
vi. Substrate deficiency
<ul style="list-style-type: none"> <li>• Malnutrition</li> <li>• Pregnancy</li> </ul>

**Table 1.89:** Factors responsible for hypoglycaemia in diabetes

The factors are:	
1.	Intake of too little food or no food but insulin is taken as regular
2.	Unaccustomed exercise is attempted but preceding dose of insulin is not reduced
3.	Alcohol intake
4.	Poorly designed insulin regimen. There is mismatch between insulin administration and food habits
5.	Defective counter-regulatory mechanisms such as release of glucagon and catecholamines in diabetes. They are anti-insulin in action.
6.	Impaired gastric emptying. This produces mismatch between intake of food and insulin action
7.	Malabsorption of food
8.	Factitious (self-induced) hypoglycaemia
9.	An unrecognised low renal threshold for glucose. Attempts to render the urine sugar-free will inevitably produce hypoglycaemia
10.	Renal failure. The kidneys are important sites for the clearance of insulin which tends to accumulate if renal failure is present.

<45 mg% while others may not appreciate the symptoms even when blood glucose level is less than 40 mg%.

**Table 1.90:** Symptoms and signs of hypoglycaemia

• <b>CVS:</b> Palpitation, tachycardia, anxiety cardiac arrhythmias
• <b>CNS:</b> Tremors, confusion, headache, tiredness, difficulty in concentration, incoordination, slurred speech, drowsiness, convulsions, plantar extensors, coma
• <b>GI tract:</b> Nausea, vomiting
• <b>Skin:</b> Sweating, hypothermia

Occasionally, a few patients feel symptoms when blood sugar is even > 45 mg%. Actually these are the patients who are aware of these symptoms, hence may feel them early before glucose levels fall to low levels. The mechanism of this variation is not understood. Hypoglycaemia is reversible with administration of glucose, symptoms and signs may disappear rapidly if it is insulin induced but may take sometime if induced by oral hypoglycaemics.

### 352. What are the differences between diabetic and hypoglycemic coma?

**Ans.** Differentiation between hyperglycaemic and hypoglycaemic coma are tabulated in Table 1.91.

**Table 1.91:** Hypoglycaemic vs diabetic coma

Features	Hypoglycaemic coma	Diabetic coma
<b>History</b>	Regular dose of insulin and no food	Too little or no insulin but food is taken as regular
<b>Precipitating factor</b>	Severe unaccustomed exercise	Untreated/hidden infection
<b>Symptoms</b>	No vomit/occasional vomit	Frequent vomiting with abdominal pain
<b>Physical signs</b>	<ul style="list-style-type: none"> <li>• Skin and tongue moist</li> <li>• Pulse is bounding</li> <li>• Normal breathing</li> <li>• No air hunger</li> <li>• No abnormal smell of breath</li> <li>• Tendon reflexes brisk</li> <li>• Plantars are extensor</li> </ul>	<ul style="list-style-type: none"> <li>• They are dry due to dehydration</li> <li>• Weak/feeble pulse</li> <li>• Rapid shallow breathing (kussmaul)</li> <li>• Air hunger present</li> <li>• Smell of acetone</li> <li>• Diminished</li> <li>• Plantars are normal (flexor)</li> </ul>
<b>Urine examination</b>	No glucose, no ketone	Glucose and ketones bodies are present
<b>Blood</b>	Low blood glucose Bicarbonate level and pH normal	High blood glucose Low bicarbonate and pH.

**CASE 27: AORTIC STENOSIS (AS)**

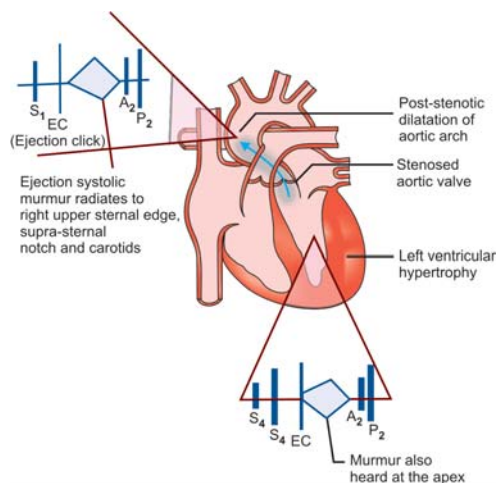
The patient (not shown) present with history of exertional dyspnoea and off and on chest pain. There was history of pain in right hypochondrium and oedema legs and feet. The auscultatory findings of the patient are depicted in the Fig. 1.27A.

**Points to be noted on history**

- Exertional dyspnoea
- Angina pectoris
- Cough, hemoptysis, dyspnoea, orthopnoea, PND due to left heart failure
- Exertional syncope due to low cardiac output
- Sudden death

**General physical examination**

- Pulse is low volume, anacrotic, slow rising
- Pulse pressure is low
- Jugular venous pressure is raised if right heart failure develops. Prominent 'a' wave may be seen
- Ankle edema may be present if heart failure develops



**Fig. 1.27A: Aortic stenosis. Auscultatory findings and haemodynamic consequences**

**Clinical Presentations**

1. Asymptomatic. It may be asymptomatic, detected on examination as an incidental finding. Congenital or mild. AS remain asymptomatic throughout life
2. Patients of moderate or severe AS may complain of palpitation, dyspnoea, anginal pain etc.
3. Patients with severe AS may also complain of syncope or giddiness and vertigo.

**Systemic examination****Inspection**

- Apex beat may be normally placed or displaced down beyond left 5th intercostal space outside the mid-clavicular line due to left ventricular hypertrophy/ enlargement. It is forceful and sustained.

**Palpation**

- Apex beat may be normally placed or displaced downwards and outwards due to left ventricular hypertrophy. It is forceful and sustained (heaving)
- Left ventricular thrust may be palpable
- P<sub>2</sub> may become palpable if pulmonary hypertension develops.

**Percussion**

- Cardiac dullness is within normal limits.

**Auscultation**

- A mid-systolic ejection murmur which is diamond-shaped (crescendo-decrescendo) often with thrill best heard at right 2nd space (A<sub>1</sub> area) or left 3rd space (A<sub>2</sub> area), is radiated to carotid vessels and downwards to apex. Murmur is best heard in sitting position with patient bending forward. An ejection click (EC) is heard in valvular aortic stenosis (Fig. 1.27A). Second heart sound is short and feeble, normal or paradoxically split.
- **Other systems examination**
  1. **Respiratory system**  
Basal rales at both the bases of the lungs
  2. **Abdomen**
    - Hepatomegaly may be present
    - No ascites, no splenomegaly

**353. What is aortic stenosis? What are its types?**

**Ans.** Aortic stenosis is defined as narrowing of the aortic orifice due to valve or wall involvement leading to left ventricular outflow obstruction (pressure overload).

**Types and Forms**

1. **Valvular aortic stenosis (bicuspid aortic valve).** It is the commonest type of congenital aortic stenosis.
2. **Congenital subvalvular AS.** This congenital anomaly is produced by either a membranous diaphragm or a fibrous ridge just below the aortic valve, or asymmetrical hypertrophy of the interventricular septum—called idiopathic hypertrophic subaortic stenosis (IHSS).
3. **Supravalvular AS.** This uncommon congenital anomaly is produced by narrowing of the ascending



aorta or by a fibrous diaphragm with a small opening just above the aortic valve. It is commonly seen in William's syndrome (Table 1.92).

**Table 1.92:** William's syndrome

- *Elfin facies*, e.g. broad forehead, pointed chin, upturned nose, hypertelorism, peg-shaped incisors, low set ears.
- Supravalvular aortic stenosis
- Mental retardation
- Hypercalcaemia

### 354. What are causes of aortic stenosis?

**Ans.** The likely aetiology varies with the age of the patient. The possible causes are summarised in Table 1.93.

**Table 1.93:** Causes of aortic stenosis

- 1. Infants, children, adolescents**
  - Congenital aortic stenosis (valvular)
  - Congenital subvalvular aortic stenosis
  - Congenital supravalvular aortic stenosis
- 2. Young adults and middle-aged persons**
  - Calcification and fibrosis of congenitally bicuspid aortic valve
  - Rheumatic aortic stenosis
- 3. Old age**
  - Senile degenerative aortic stenosis
  - Calcification of bicuspid valve
  - Rheumatic aortic stenosis

### 355. What are important features of aortic stenosis?

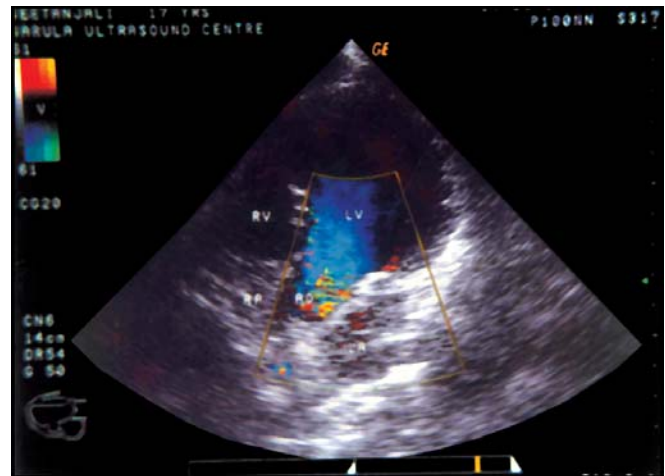
**Ans.** Common features of AS are:

- Dyspnoea, angina and syncope on exertion
- Slow rising sustained low volume pulse called anacrotic pulse
- Low systolic pressure with low pulse pressure (< 20 mmHg)
- Apex beat down and out or may be normal with heaving in character
- Cardiomegaly
- Ejection click and ejection systolic murmur and a thrill in aortic area conducted to carotids. The same murmur is also heard at apex
- Basal crackles and rales. Signs of pulmonary congestion may be present (LVF).

### 356. How will you investigate a patient with AS?

**Ans.** Following investigations are done:

- 1. Electrocardiogram (ECG)** may show left atrial and left ventricular hypertrophy with strain, i.e. ST-T wave changes due to myocardial ischemia may be present. Left bundle branch block may occur sometimes.
- 2. Chest X-ray:** It may be normal. Sometimes, heart is enlarged due to a left ventricular hypertrophy. Post-stenotic dilatation of aorta may be seen in some cases. Lateral view may show calcification of aortic valve.
- 3. Echocardiography (Fig. 1.27B).** It will show left ventricular enlargement and hypertrophy, calcification of valve and decreased left ventricular function.
- 4. Doppler echocardiography:** demonstrates the systolic gradient across the valve, detects presence and absence of aortic regurgitation.



**Fig. 1.27B:** Aortic stenosis. Color Doppler Echocardiogram showing aortic stenosis with gradient of 50 mm across the valve

### 357. How will you differentiate among three common types of AS?

**Ans.** The differential diagnosis of aortic stenosis lies among its three types:

- 1. Valvular AS** (its important features have already been listed)
- 2. Subvalvular aortic stenosis** (idiopathic hypertrophic subaortic stenosis –IHSS). The features are:
  - Dyspnoea, angina pectoris, fatigue and syncope
  - Double apical impulse (apex beat)
  - A rapidly rising carotid arterial pulse



- Pulsus bisferiens (double upstroke)
- A harsh, diamond-shape ejection systolic murmur without ejection click is best heard at lower left sternal border as well as at the apex. It does not radiate to neck vessels. It becomes louder with valsalva manoeuvre.
- Early diastolic murmur of aortic regurgitation may also be heard in some patients.
- No post-stenotic dilatation
- Second heart sound is normal, single.

### 3. Supraaortic stenosis

- Unequal BP in both arms, i.e. right arm > left arm
- May be associated with other features of William's syndrome
- No ejection click, only ejection systolic murmur
- Systolic thrill is more pronounced and radiates to the neck vessels but not to the apex
- A<sub>2</sub> is accentuated
- No poststenotic dilatation.

### 358. What are the complications of AS?

**Ans.** Common complications are as follows:

- Left ventricular failure
- Congestive cardiac failure
- Infective endocarditis
- Arrhythmias
- Precipitation of angina
- Sudden death. It is more common in hypertrophic cardiomyopathy (HOCM).

### 359. How will you differentiate between aortic stenosis and pulmonary stenosis?

**Ans.** Differences between AS and PS are dealt with in Table 1.94.

### 360. What are characteristics of severe aortic stenosis?

**Ans.** Aortic stenosis is said to be severe when:

- Pulse character is slowly rising plateau
- Pulse pressure is narrow
- Signs of LVF present
- S<sub>2</sub> is soft, single or paradoxically split
- Presence of S<sub>4</sub>
- Systolic thrill and late peaking of ejection systolic murmur

**Table 1.94:** Differentiation between aortic stenosis and pulmonary stenosis (PS)

Features	AS	PS
Pulse	Small amplitude, anacrotic, parvus or tardus	Normal
BP	Low systolic	Normal
Apex beat	Heaving	Normal
Second heart sound	A <sub>2</sub> soft	P <sub>2</sub> soft
Splitting of S <sub>2</sub>	Reverse	Wide
Location of systolic murmur	Aortic area, conducted to carotids	Pulmonary area. No conduction
Relation to respiration	No change	Increases on inspiration
Associated ventricular hypertrophy	LVH	RVH

- Cardiac catheterisation reveals transvalvular gradient >60 mmHg

### 361. What are causes of systolic murmur in aortic and pulmonary area?

**Ans.** The murmurs in this area are ejection or mid systolic. The causes of ejection systolic murmur (ESM) are given in Table 1.95.

**Table 1.95:** Systolic murmurs at base of the heart

<b>Aortic area (A1 and A2) (right 2nd and left 3rd space)</b>
<ul style="list-style-type: none"> <li>• AS</li> <li>• Systemic hypertension</li> <li>• Coarctation of the aorta</li> <li>• Aneurysm of the ascending aorta</li> <li>• Atherosclerosis of the aorta (old age)</li> <li>• Functional flow murmur in AR</li> </ul>
<b>Pulmonary area (left 2nd interspace)</b>
<ul style="list-style-type: none"> <li>• Pulmonary stenosis</li> <li>• Pulmonary hypertension</li> <li>• Cor pulmonale (acute or chronic)</li> <li>• Hyperkinetic states, e.g. anaemia, thyrotoxicosis, fever, pregnancy</li> <li>• Congenital heart diseases, e.g. ASD, VSD, Fallot's tetralogy</li> <li>• Innocent (benign) murmur</li> </ul>

**362. What are benign (innocent) murmurs?**

**Ans.** These murmurs are flow murmurs without organic cause, commonly seen in children due to;

- Hyperkinetic circulatory state in children especially during exercise, crying or fever.
- Increased resistance of the pulmonary vascular bed

*Characteristics:*

- Usually systolic localised to pulmonary outflow tract
- There is no associated thrill
- Best heard in supine position, may disappear in upright position
- Heart sounds are normal.

**363. What is a hemic murmur?**

**Ans.** It is an ejection systolic murmur heard at the pulmonary area due to rapid blood flow in a patient with severe anaemia. It is due to hyperkinetic circulatory state combined with dilatation of pulmonary artery and its vasculature.

Note: hemic murmurs are also functional ejection systolic murmur similar to heard in various hyperkinetic states.

**364. What are functional murmurs?**

**Ans.** These murmurs occur in the absence of organic heart disease, are due to turbulence produced by rapid flow of blood across a normal valve. These may be systolic and diastolic (Table 1.96). These murmurs are not loud, are localised in nature, and usually not associated with thrill. They are haemodynamically insignificant, do not produce cardiomegaly.

**Table 1.96:** Functional murmurs

<i>Systolic</i>
<ul style="list-style-type: none"> <li>• Systolic murmur across pulmonary valve in left to right shunt, e.g. ASD, VSD</li> <li>• Functional systolic murmur in aortic area in patients with severe AR</li> </ul>
<i>Diastolic</i>
<ul style="list-style-type: none"> <li>• Graham-Steell murmur (early diastolic) due to pulmonary regurgitation in pulmonary hypertension</li> <li>• Apical mid-diastolic murmur (Austin-Flint murmur) in severe AR.</li> </ul>

**CASE 28: AORTIC REGURGITATION (AR)**

A patient (not shown) presented with palpitation, dyspnoea and off and on chest pain. The auscultatory findings are depicted in the Fig. 1.28. The patient had mild oedema feet.

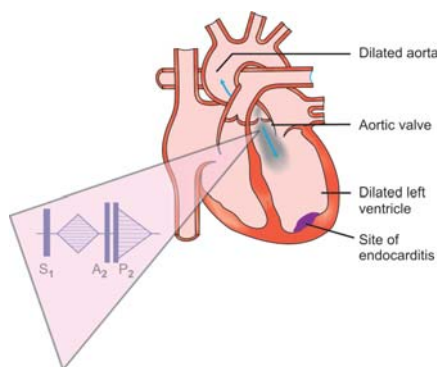
**History—points to be noted**

- Onset of symptoms and their course
- Ask the history of cough, dyspnoea, orthopnoea, PND
- Ask for history of haemoptysis, anginal pain, headache
- History of fever
- History of oedema feet and legs
- History of loss of function of any part, i.e. paralysis
- Past history of sore throat, skin infection or arthralgia (fleeting) or joint pain (arthritis).

**General physical examination**

- Face for appearance, i.e. dyspnoeic or orthopnoeic, ill-look. Note puffiness or facial oedema
- Mouth. Look the tongue and mucous membrane for anaemia or bleeding or evidence of infection, high-arch palate
- Neck examination for venous pulsations, arterial pulsation (read below) and JVP, lymph nodes
- Pulse, BP, respiration and temperature
- Note the following other peripheral signs in case of AR
- Collapsing or good volume pulse (wide pulse pressure)
- Bounding peripheral pulses
- Dancing carotids (Corrigan's sign)
- Capillary pulsations in nail beds (Quinke's sign)
- Pistol shots sound and Duroziez's sign/murmur
- Head nodding with carotid pulse—Mussel's sign
- Hill's sign (BP in lower limb > upper limbs)
- Cyanosis (peripheral, central or both) may be present
- Pitting ankle oedema may be present
- Tender hepatomegaly if right heart failure present.

*All these peripheral signs may not be evident in mild AR. In our case, they were present indicating severe AR.*



*Lean the patient forward with breath held in expiration to hear the early diastolic murmur, best heard in A<sub>2</sub> area (left 2nd intercostal space)*

**Fig. 1.28: Aortic regurgitation**

**AORTIC REGURGITATION (AR)****Clinical Presentations**

- I. *Mild to moderate AR*
  - Often asymptomatic
  - Palpitation—pounding of heart is a common symptom
  - Symptoms of left heart failure appear but late
- II. *Severe AR*
  - Symptoms of heart failure, i.e. dyspnoea, orthopnoea, PND are present at onset
  - Angina pectoris is frequent complaint
  - Arrhythmias are uncommon.

**Examination of CVS****Inspection**

- Apex beat is displaced down and outside the midclavicular line and is forceful
- Left ventricular thrust
- Pulsations in suprasternal notch and epigastrium are usually seen.

**Palpation**

- Apex beat is forceful and sustained
- No thrill is palpable
- Tender hepatomegaly if right heart failure present.

**Percussion**

- Cardiac dullness is within normal limits.

**Auscultation**

- An *early diastolic murmur* is best heard in A<sub>2</sub> area (3rd left intercostal space) or A<sub>1</sub> area (2nd right intercostal space) in sitting position with patient leaning forward and during held expiration
- An *ejection systolic murmur* in the same area. It is due to increased stroke volume. It may also radiate to neck vessels
- *Austin flint* (soft, middiastolic) murmur at apex in severe AR.
- Second heart sound is soft and feeble
- Signs of left heart failure (fine end-inspiratory rales at bases of lungs).

**Table 1.97:** Signs and symptoms of aortic regurgitation (AR)

Symptoms	Signs of moderate to severe AR
<p><i>Mild to moderate AR</i></p> <ul style="list-style-type: none"> <li>• Often asymptomatic</li> <li>• Palpitation- pounding of heart is a common symptom</li> <li>• Symptoms of left heart failure appear but late</li> </ul> <p><i>Severe AR</i></p> <ul style="list-style-type: none"> <li>• Symptoms of heart failure, i.e. dyspnoea, orthopnoea, PND are present at onset</li> <li>• Angina pectoris is frequent complaint</li> <li>• Arrhythmias are uncommon</li> </ul>	<p><i>Peripheral signs*</i></p> <ul style="list-style-type: none"> <li>• Collapsing or good volume pulse (wide pulse pressure)</li> <li>• Bounding peripheral pulses</li> <li>• Dancing carotids (<i>Corrigan's sign</i>)</li> <li>• Capillary pulsation in nail beds (<i>Quincke's sign</i>)</li> <li>• Pistol shot sound and <i>Duroziez's sign/ murmur</i></li> <li>• Head nodding with carotid pulse <i>de Musset's sign</i></li> <li>• <i>Hill's sign</i> (BP in lower limbs &gt; upper limbs)</li> <li>• Cyanosis (peripheral, central or both) may be present</li> <li>• Fundus examination will reveal capillary pulsations</li> <li>• Pitting ankle oedema may be present</li> <li>• Tender hepatomegaly if right heart failure present</li> </ul>
<p>*All these peripheral signs may not be evident in mild AR because these indicates wide pulse pressure due to significant aortic run-off into the heart.</p>	

### 365. What is your provisional diagnosis. In this case?

**Ans.** In view of clinical features and auscultatory findings, the provisional diagnosis is aortic regurgitation with congestive cardiac failure without evidence of endocarditis or thromboembolic complication. The cause of AR is to be found out.

### 366. Is it severe or mild to moderate AR?

**Ans.** The presence of all the signs of wide pulse pressure indicate severe AR in this patient. However, the signs and symptoms depending on severity are described in Table 1.97 and clinical examinations and clinical features presented in Table 1.98 and Figure 1.28, respectively.

### 367. How do you define AR?

**Ans.** When blood is pushed by left ventricle into the aorta during systole, a part of it regurgitates back into same ventricle during diastole due to inadequate closure of the aortic valve, called *aortic regurgitation*. It leads to volume overload of the left ventricle resulting in its hypertrophy and enlargement.

### 368. What are its causes?

**Ans.** The causes are:

- I. Congenital
  - Bicuspid valve
- II. Acquired
  - Rheumatic heart disease
  - Infective endocarditis (acute regurgitation)
  - Trauma leading to valve rupture

**Table 1.98:** Examination of CVS

#### Inspection

- Apex beat is displaced down and outside the midclavicular line and is forceful
- Left ventricular thrust
- Pulsations in suprasternal notch and epigastrium are usually seen
- Pulmonary artery pulsation in second left intercostal space may be visible

#### Palpation

- Apex beat is forceful and sustained (heaving)
- No thrill is palpable
- Left parasternal heave present
- Tender hepatomegaly if right heart failure develops

#### Percussion

- Cardiac dullness corresponds with the apex beat

#### Auscultation

- An early diastolic murmur is best heard in A<sub>2</sub> area (3rd left intercostal space) or A<sub>1</sub> area (2nd right intercostal space) in sitting position with patient leaning forward and during held expiration (Fig. 1.28)
- An ejection systolic murmur in the same area. It is due to increased stroke volume. It may also radiate to neck vessels. It is present only when severe AR is present
- Austin-Flint (soft mid-diastolic) murmur at apex in severe AR
- Second heart sound is soft and feeble
- Signs of left heart failure (fine end-inspiratory rales at bases of lungs)

- Atherosclerosis
- Marfan's syndrome (aortic dilatation)
- Syphilitic aortitis
- Ankylosing spondylitis, rheumatoid arthritis
- Dissecting aneurysm of ascending aorta.

**Table 1.99:** Differential diagnosis of AR

<i>Rheumatic AR</i>	<i>Syphilitic AR</i>	<i>Aortic dilatation (Marfan's syndrome)</i>
Young age group	Older age group	Young age
History of rheumatic fever in the past	History of sexual exposure	Eunuchoidism (lower segment > upper segment, arachnodactyly)
Other valves may be involved	Usually an isolated lesion	Mitral valve may be involved (floppy mitral valve syndrome)
Diastolic thrill absent	Thrill may be present	Aortic pulsation in suprasternal notch. No thrill
A <sub>2</sub> diminished or absent	A <sub>2</sub> may be loud (tambour like)	A <sub>2</sub> normal
Murmur best heard in left 3rd space (A <sub>2</sub> area)	Murmur best heard in right second or 3rd space along right sternal border	Murmur heard in second right and third left intercostal space
Peripheral signs present	Peripheral signs are marked, Austin-Flint murmur may be present	Peripheral signs are usually absent.

**Causes of Acute AR**

- Acute bacterial endocarditis
- Trauma to the chest
- Acute dissection of the aorta.

**369. What are clinical features of acute AR?**

**Ans.** The clinical features of acute AR will be:

- An acutely ill patient with severe breathlessness, chest discomfort
- Acute left ventricular failure (LVF)
- Peripheral signs of AR will be absent.

**370. Differential diagnosis of AR.**

**Ans.** The common causes of AR are compared clinically in the Table 1.99.

**371. What are differences between AR and PR (pulmonary regurgitation)?**

**Ans.** These are summarised in Table 1.100.

**372. How will you decide whether MDM in mitral area is due to severe AR or due to associated MS?**

**Ans.** The mid-diastolic murmur in AR may be confused with MDM of MS though both lesions may coexist. The differentiation are given in Table 1.101.

**373. How will you investigate a patient with AR?**

**Ans.** Following investigations are done:

1. Chest X-ray (PA view) may show;
  - Cardiomegaly (LV enlargement-boot shaped heart)

**Table 1.100:** Differentiation between AR and PR

<i>Feature</i>	<i>AR</i>	<i>PR</i>
Peripheral signs of wide pulse pressure	Present	Absent
Apex beat	Hyperdynamic	Normal
Site of early diastolic murmur	Best heard in aortic area	Best heart in pulmonary area
Relation of murmur to respiration	None	Increases with inspiration
Ventricular enlargement		LVH RVH

**Table 1.101:** Differential diagnosis of MDM in AR

<i>Feature</i>	<i>Severe AR (Austin-Flint murmur)</i>	<i>AR with MS</i>
Peripheral signs of AR	Florid	Masked
Character of murmur	Soft	Rough and rumble
First heart sound (S <sub>1</sub> )	Normal	Loud
Opening snap (OS)	Absent	Present
LA enlargement	Absent	Present
Calcification of mitral valve	Absent	May be present
Echocardiogram	Normal	Suggestive of MS

- Dilatation of ascending aorta
  - Aortic knuckle prominent
2. ECG may show
    - LVH and left atrial hypertrophy in moderate to severe AR



- ST segment depression and T wave inversion due to left ventricular strain
3. *Echocardiogram. It detects;*
- Left ventricular enlargement, hyperdynamic left ventricle
  - Fluttering of anterior mitral leaflet in severe AR
  - Aortic root dilatation
  - Vegetations may be detected in a case with endocarditis
  - Assessment of LV function
4. *Colour Doppler flow studies* detect the reflux through aortic valve and its magnitude

### 374. What are complications of AR?

**Ans.** Following are common complications:

- Acute LVF
- Infective endocarditis
- CHF
- Cardiac arrhythmias
- Heart blocks (calcific aortic valve)
- Precipitation of angina.

### 375. What are the causes of an ejection systolic murmur in aortic area? How will you differentiate them?

**Ans.** The ejection systolic murmur in aortic area occurs either in severe AR or when AR is associated with AS or

isolated AS. The AS has already been discussed. The differences between severe AR or AR with AS are compared in Table 1.102.

**Table 1.102:** Differential diagnosis of an ejection systolic murmur (ESM) in AR

Feature	Severe AR	AR with AS
Signs of wide pulse pressure (water-hammer pulse, Corrigan's sign, dancing carotids and pistol shot sounds etc).	Present	Absent
Systolic BP	High systolic	Normal or low systolic
Ejection click	Absent	Present
Radiation of murmur	Usually localised, may radiate to neck vessels	Widely radiated to neck vessels as well as to apex
Systolic thrill	Absent	Present

### 376. How will you decide the dominance of a lesion in combined AS and AR?

**Ans.** The features of dominant AS or AR in combined aortic lesion are given in Table 1.103.

**Table 1.103:** Dominant aortic stenosis vs aortic regurgitation in combined AS and AR

Features	Dominant AS	Dominant AR
I. Symptoms	All are marked	Chest pain, dyspnoea, palpitation common
• Exertional angina		
• Dyspnoea on effort		
• Fatigue		
• Syncope		
• Palpitation		
II. Signs		
Pulse	Low volume Pulsus bisferiens (tidal wave prominent than percussion wave)	High volume collapsing pulse Pulsus bisferiens (percussion wave prominent than tidal wave)
BP	• Low systolic BP • Low pulse pressure	• High systolic BP • Wide pulse pressure
Peripheral signs of AR	Masked	Marked
Apex beat	Heaving	Hyperdynamic
Thrill	Systolic	No thrill
S <sub>3</sub>	Absent	Present
S <sub>4</sub>	May be present	Absent
Ejection click	Present	Absent
Diastolic murmur	Short early diastolic	Prominent early diastolic
Systolic murmur	Marked, radiating to neck vessels	Present, does not radiate to neck vessels

## CASE 29: MITRAL STENOSIS

The patient (not shown) presented with off and on cough and expectoration with dyspnoea and PND for the last 4-5 years. There was history of pain abdomen, oedema feet and haemoptysis off and on. His auscultatory findings are depicted in Fig. 1.29.

## History—points to be noted

- History of orthopnoea, PND
- Any history of pain chest, haemoptysis
- History of dizziness, vertigo or syncope
- History of fever, joint pain or urinary disturbance
- History of pain abdomen, oedema feet or legs
- History of any paralysis (motor or sensory deficit)
- History of missing of heart beat.

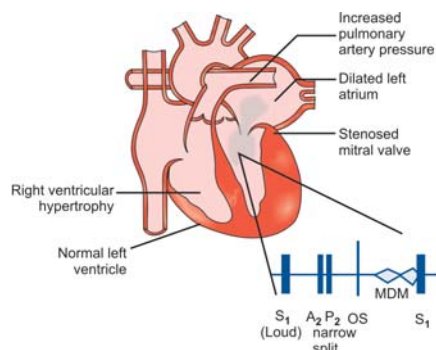
## Past history

- History of sore throat, joint pain, rash or abnormal movement or skin infection
- History of recurrent chest pain or haemoptysis.

## Physical Signs

- Mitral facies – A characteristic bilateral, cyanotic or dusky pink hue (malar flush) on cheeks.
- Low volume pulse, which may be irregularly irregular if atrial fibrillation is present.
- Low pulse pressure
- Raised jugular venous pressure and 'a' wave on jugular venous pulse will be absent in atrial fibrillation
- Cold extremities: Extremities are usually warm but may be cold in severe mitral stenosis or due to embolisation.
- Pitting ankle oedema

*Note:* Always look for the signs of bacterial endocarditis (Read Case 31) or acute rheumatic activity in a case of MS, if complicated.



**Fig. 1.29:** Mitral stenosis. Hemodynamic effects and auscultatory findings in MS Roll the patient to the left to hear MDM (low pitched mid-diastolic rumbling murmur, which is best heard with the bell of stethoscope)

## Clinical Presentations

1. The patients of mild MS may be asymptomatic and a presystolic murmur may be an evidence which increases on exercise.
2. Patients of mild to moderate MS present with symptoms of low cardiac output, e.g. syncope, fatigue, weakness. They may have exertional dyspnoea only.
3. Patients of moderate to severe MS present with symptoms and signs of left heart failure followed by right heart failure and congestive cardiac failure.
4. These cases of MS of any severity may present with features of embolisation (e.g. hemiplegia, recurrent haemoptysis, gangrene of peripheral parts) due to thrombus either in left atrium or peripheral venous system; the formation of which is triggered by either a transient arrhythmias (e.g. AF) or LVF or CHF.

## I. Estimation of Heart (CVS)

## Inspection

- Apex beat is normally situated
- Apex beat is displaced outwards but not downwards
- Pulsation of pulmonary artery may be visible in 2nd left intercostal space.
- Epigastric pulsations may be visible due to right ventricular hypertrophy.
- Left parasternal lift may be visible.

## Palpation

- Apex beat is palpable and tapping in character
- An apical diastolic thrill may be palpable in left lateral position
- 1st heart sound at apex (mitral area) may become palpable, best demonstrated in left lateral position.
- Parasternal heave is usually present
- Second sound (pulmonary component) may become palpable at left 2nd intercostal space
- Right ventricular pulsations may be palpable in epigastrium.

## Percussion

- Left border of heart corresponds with apex beat
- 2nd and 3rd left intercostal spaces may become dull due to pulmonary hypertension.

## Auscultation

## 1. Mitral area (apex)

- Heart beats may be irregular due to atrial fibrillation
- First heart sound is loud and banging, short and snappy
- A mid-diastolic murmur, best heard in left lateral position with the bell of stethoscope. It is rough and rumble. It is accentuated during late diastole called 'presystolic accentuation'. A presystolic murmur without mid-diastolic murmur is an early sign of mitral stenosis, and in mild mitral stenosis this may be the only finding.

- Opening snap (OS) is present. It is snapping sound heard after 2nd heart sound. Its proximity to  $S_2$  determines the severity of mitral stenosis. Nearer the opening snap to 2nd heart sound, more severe is the mitral stenosis. It is absent if valve becomes calcified.

**2. Pulmonary area** (left 2nd intercostal space)

- Loud 2nd heart sound due to pulmonary arterial hypertension
- There may be an ejection systolic or an early diastolic murmur (Graham-Steell murmur) due to pulmonary regurgitation.
- Splitting of 2nd heart sound becomes narrow

**3. Tricuspid area** (lower left para-sternal border)

There may be a pansystolic murmur due to functional tricuspid regurgitation which may develop in cases with severe mitral stenosis.

**4. Aortic area** (right 2nd intercostal space)

Normal 2nd heart sound heard. No abnormality detected in this area.

## II. Examination of Other Systems

**(i) Examination of lungs**

There may be fine crepitations (end-inspiratory crackles) at both the bases of lungs due to LHF. There may be hydrothorax (pleural effusion)

**(ii) Examination of abdomen**

Liver is enlarged, soft and tender. Ascites may be present. Spleen gets enlarged in presence of subacute bacterial endocarditis.

**(iii) Examination of nervous system**

- Monoplegia/hemiplegia due to embolism
- Sydenham's chorea
- Optic fundi for Roth's spots.

**377. What is the clinical diagnosis?**

**Ans.** In view of symptoms and physical signs described in this case, the patient appears to have RHD with MS, sinus rhythm (say AF if present), CHF without infective endocarditis or acute rheumatic activity.

**378. What are common features of MS?**

**Ans.** The common features of MS and their pathogenesis is described in the Box 1.2.

**379. What are the common causes of mitral stenosis?**

**Ans.** The causes are:

1. *Rheumatic*, MS is invariably rheumatic in origin.
2. *Congenital*, e.g. parachute mitral valve where all chordae tendinae are inserted into a single papillary muscle
3. Rarely- carcinoid syndrome, SLE, endomyocardial fibrosis, Hurler's syndrome.

**Box 1.2:** Clinical manifestations of MS

- 1. Symptoms due to low cardiac output, e.g.**
  - fatigue
  - tiredness
  - weakness
  - lethargy
- 2. Symptoms of pulmonary congestion (left heart failure), e.g.**
  - dyspnoea,
  - orthopnoea,
  - paroxysmal nocturnal dyspnoea (PND)
  - haemoptysis
- 3. Symptoms of right heart failure, e.g.**
  - puffiness of face and oedema of legs
  - pain in right hypochondrium due to hepatomegaly
- 4. Symptoms due to embolisation, e.g.**
  - right sided embolisation leads to haemoptysis and pain chest
  - left sided or systemic embolisation leads to hemiplegia, acute pain abdomen (infarction of viscera), loss of peripheral pulses or gangrene, etc.
- 5. Symptoms related to arrhythmias, e.g.**
  - palpitation,
  - missing of beat(s).

**380. How do you define mitral stenosis? What are its hemodynamic consequences?**

**Ans.** The normal mitral valve orifice is 4-6 cm<sup>2</sup> (average 5 cm<sup>2</sup>) in diastole in adults. Narrowing of the mitral valve is called *mitral stenosis*. The symptoms arise due to haemodynamic disturbances such as rise in left atrial pressures, pulmonary arterial pressure when valve orifice is reduced to half of its original size (2.0 cm<sup>2</sup> approx). Mitral stenosis is severe when orifice is 1cm<sup>2</sup> or less and said to be *critical*. The haemodynamic consequences in severe stenosis include rise in left atrial, pulmonary venous pressure and pulmonary oedema (LVF) followed by pulmonary arterial hypertension and right heart failure. This is called *backward failure theory of heart failure*.

*Functional Mitral Stenosis* refers to functional obstruction to inflow of blood from left atrium to left ventricle, is due to rapid flow through a normal valve as seen in (i) hyperdynamic circulation (VSD, ASD, PDA, thyrotoxicosis, anaemia etc) and (ii) in severe mitral regurgitation. Severe aortic regurgitation produces functional MS by partially narrowing the valve by regurgitant jet.

In organic lesion, the valve is deformed while in functional MS, the valve is normal.

**381. How do you diagnose MS? What are points that favor diagnosis of MS?**

**Ans.** Characteristics of mitral stenosis are as follows:

1. *Palpable apex beat*. Apex beat is palpable and tapping in character (tapping character is due to palpable first heart sound)
2. *Loud first heart sound (S<sub>1</sub>)*. Due to persistent rise in left atrial pressure, the diastolic gradient across the mitral valve is increased that keeps the valve cusps wide open at the end of diastole with the result when ventricular systole starts, the widely opened mitral valve cusps close rapidly like a thud producing a loud S<sub>1</sub>.
3. *Mid-diastolic murmur (MDM) with presystolic accentuation*. The murmur is rough, rumbling, low-pitched, low frequency, of variable duration, best heard at the apex in left lateral position with bell of the stethoscope. The murmur is mid-diastolic because there is no flow of blood across mitral valve in isovolumetric relaxation phase (early diastole).

There is presystolic accentuation of the murmur. The last part of the ventricular filling in diastole depends on the atrial boost which normally is small but increased in MS due to raised left atrial pressure, hence, accentuation of the murmur.

4. *Opening snap (OS)*. This is a snappy, sound produced due to sudden forceful opening of the mitral valve during diastole due elevated left atrial pressure. It is heard in expiration with diaphragm of stethoscope at or just medial to cardiac apex. This sound follows aortic component of second heart sound (A<sub>2</sub>) by 0.05 to 0.1 sec.

**Significance**

- The presence of OS indicates organic MS
- The OS indicates that mitral valve is still pliable (i.e. not calcified). It disappears if valve is calcified
- It also decides the severity of MS. Diminishing A<sub>2</sub>-OS gap (gap between second heart sound and OS) indicates increasing severity of the MS.
- It disappears following valvotomy.

**Table 1.104:** Diseases /conditions causing muffling of  $S_1$  in MS

Diseases/condition	Mechanism
1. Mitral regurgitation or aortic regurgitation	Valve cusps do not close properly due to dilatation of the valve ring
2. Mitral valve calcification	Valve cusps are immobile
3. Acute rheumatic carditis and digitalis toxicity or overdosage	P-R interval is prolonged
4. Myocardial infarction or dilated heart (gross CHF)	The valve does not close completely as the forces that close the valve are diminished
5. Emphysema, pericardial effusion, obesity, rotation of the heart	All these conditions do not affect the mitral valve, hence production of $S_1$ is normal, but its transmission through the chest is diminished.

Note: Atrial fibrillation and complete heart block produce varying intensity of the first heart sound

### 382. What are the causes of loud $S_1$ ?

**Ans.** Following are causes:

- Mitral stenosis
- Tricuspid stenosis
- In tachycardia.  $S_1$  is loud due to short P-R.
- Hyperkinetic circulation (exercise, anaemia, thyrotoxicosis, fever, pregnancy, etc). This is due to rapid flow across the valves which keeps them wide open (functional MS), hence, their closure produces loud  $S_1$ .
- Short P-R interval. P-R interval influences the heart rate, short P-R causes loud  $S_1$  while long P-R causes muffling of  $S_1$ . The short P-R interval is seen in WPW syndrome and in tachycardias.
- Children or young adults (physiological)

### 383. What are the causes of muffling of $S_1$ in MS? What are the causes of changing $S_1$ ?

**Ans.** Certain conditions/diseases when associated with MS produce muffling of  $S_1$  (Table 1.104). The causes of changing 1st sound are given in the footnote of the table.

### 384. What are causes of mid-diastolic murmur (MDM) at the apex?

**Ans.** In addition to MS, the other conditions/diseases that lead to mid-diastolic murmur are;

1. *Active rheumatic carditis (valvitis)*. It produces a soft mid-diastolic (Carey-Coomb's) murmur without loud  $S_1$ , opening snap and diastolic thrill. It is due to oedema of valve cusps just producing obstruction. The murmur disappears as soon as the acute condition is over.

2. *Severe aortic regurgitation* (Austin-Flint murmur). It is due to functional MS produced by the aortic regurgitant jet striking against the anterior mitral leaflet forcing its partial closure. The murmur has following characteristics;

- It is neither associated with loud  $S_1$  or presystolic accentuation
- Opening snap is absent
- No thrill
- The patient has florid signs of severe AR (read aortic regurgitation)

3. *Functional mid-diastolic murmur* (increased flow through a normal valve). This is seen in left to right shunts (VSD, ASD, PDA) or in hyperdynamic circulation. The murmur is soft, not associated with thrill and opening snap. The third heart sound ( $S_3$ ) due to rapid filling of the heart may be present.

4. *Severe mitral regurgitation*

- A soft mid-diastolic murmur with a pansystolic murmur and  $S_3$  indicates severe MR.

5. *Left atrial myxoma*. A pedunculated myxoma may strike against the valve in diastole producing signs of MS with mid-diastolic murmur. The characteristic features of atrial myxoma are:

- Tumour plop—a sound produced by striking of myxoma against the valve.
- Disappearance or change in the intensity and character of the murmur during lying down. The murmur is best heard in sitting position.
- No associated thrill or opening snap.
- Constitutional symptoms (fever, weight loss, arthralgia, rash) or embolic episodes may occur



- Confirmation of diagnosis is done by 2-D-echocardiography
6. *Tricuspid stenosis*. The murmur has similar characteristics as in MS, but is best heard at left sternal edge.
  7. *Ball valve thrombus*. It floats in the left atrium and produces functional MS similar to atrial myxoma from which it is differentiated by 2-D echocardiography.

### 385. What are the causes of split S<sub>1</sub>?

**Ans.** Normally the two components of 1st sound (e.g. mitral and tricuspid) cannot be heard separately. However, the S<sub>1</sub> gets split under following conditions:

- i. RBBB
- ii. Mitral or tricuspid stenosis
- iii. Ventricular pacing.

### 386. What does presystolic murmur in MS indicate? What do you mean by presystolic accentuation of MDM in MS?

**Ans.** Presystolic murmur vs presystolic accentuation of MDM in MS is as follows:

The presystolic murmur is due to forceful atrial contractions against the stenotic mitral valve. The presystolic murmur without other auscultatory findings of MS, indicates mild MS; on the other hand in sinus rhythm presystolic accentuation of the mid-diastolic murmur indicates severe mitral stenosis. Presystolic accentuation of MDM disappears in AF and big atrial thrombus.

### 387. What are the causes of opening snap?

**Ans.** Following are the causes:

- Mitral stenosis
- Tricuspid stenosis
- Left to right shunt (VSD, ASD, PDA)
- Sometimes in severe MR.

### 388. What is Lutembacher's syndrome?

**Ans.** It comprises of:

- Atrial septal defect (ASD)
- MS (rheumatic in origin)

### 389. How do you decide the severity of mitral stenosis?

**Ans.** The auscultatory findings that determine the severity of MS are:

- Lower volume pulse and low pulse pressure

- Cold peripheral extremities
- Longer duration of the mid-diastolic murmur with the pre-systolic accentuation.
- Proximity of the OS to second heart sound. More near is the OS to the aortic component of second heart sound, more severe is the MS.

### 390. What is juvenile mitral stenosis?

**Ans.** In the West, MS is seen usually in 4th or 5th decade, but in India, it develops early and may be seen in children commonly. The criteria for juvenile MS are:

- Occurs below 18 years of age
- It is usually severe (pin-point mitral valve)
- Atrial fibrillation is uncommon.
- Calcification of valve uncommon
- Needs immediate surgical correction.

### 391. What are signs of pulmonary arterial hypertension?

**Ans.** The signs are limited to second left intercostal space (pulmonary area). There is prominent a wave in neck veins which are distended. The examination of the heart shows:

*Inspection:*

- There may be visible pulmonary arterial pulsations
- Parasternal heave may be visible
- Right ventricular pulsations may be seen in epigastrium

*Palpation*

- P<sub>2</sub> may be palpable
- Left parasternal heave is palpable

*Percussion*

- The pulmonary area (second left intercostal space just lateral to sternal edge) may be dull on percussion

*Auscultation*

- P<sub>2</sub> is loud
  - Second heart sound is narrowly split
  - The *Graham Steell murmur* of pulmonary regurgitation—a high pitched diastolic decrescendo blowing murmur along the left sternal edge
  - Pulmonary ejection click
  - A soft ejection systolic murmur and right-sided S<sub>3</sub> may be heard in severe pulmonary hypertension
- Development of pulmonary hypertension is protective mechanism as it relieves pulmonary oedema.

**392. How will you investigate a case with MS?**

**Ans.** The investigations are as follows:

1. ECG: It may show left atrial hypertrophy (P mitrale), right ventricular hypertrophy and atrial fibrillation.
2. Chest X-ray: *Mitralised heart*: Left atrium is conspicuously prominent on left border of heart which is straightened. There is double atrial shadow. Signs of pulmonary congestion present. Pulmonary conus is prominent.
3. Echocardiogram shows;
  - Thickened immobile mitral cusps.
  - Reduced rate of diastolic filling (EF slope is flattened)
  - Reduced valve orifice area
  - Left atrial thrombus, if present
4. Cardiac catheterisation  
Pressure gradient between LA and LV.

**393. What are the complications of mitral stenosis?**

**Ans.** Common complications are as follows:

1. *Acute pulmonary oedema* (left heart failure). In patients with MS, the left ventricle is hypoplastic (under-filled) hence, pulmonary oedema is due to elevated left atrial pressure transmitted to pulmonary veins resulting in transudation.

In mitral stenosis, there is initial left heart failure – left atrial failure with congestion of the lungs followed by right ventricular failure or congestive heart failure

2. *Pulmonary hypertension* and *right heart failure*
3. *Arrhythmias*, e.g. atrial fibrillation, atrial flutter, VPCs
4. *Left atrial thrombus* with systemic embolisation leading to stroke, Leriche's syndrome – occlusion of bifurcation of aorta
5. *Recurrent massive haemoptysis* leading to haemosiderosis
6. *Infective endocarditis* – rare. It is common in mitral regurgitation than stenosis
7. *Recurrent pulmonary infections* due to chronic passive venous lung congestion
8. Complications produced by *enlarged left atrium*

- *Otner's syndrome*. Hoarseness of voice due to compression of recurrent laryngeal nerve.
  - Dysphagia (compression of oesophagus)
  - Clot in the left atrium gives rise to embolisation in sinus rhythm
  - Collapse of the lung due to pressure on left bronchus
9. Sudden death due to *ball valve thrombus* – a big thrombus fits like a ball into mitral valve.
  10. Interlobar effusion (*phantom tumour*) or hydrothorax (*pleural effusion*).

**394. What are clinical signs of acute pulmonary oedema?**

**Ans.** Read mitral regurgitation.

**395. What are the causes of pulmonary oedema?**

**Ans.** The pulmonary oedema may be *cardiogenic* (left ventricular or left atrial failure, high CVP, and PCWP, and engorged neck veins) or *noncardiogenic* (normal left ventricular and atrial pressure, normal CVP and PCWP and neck veins). The noncardiogenic pulmonary oedema is also called *adult respiratory distress syndrome (ARDS)*. The causes are given in Table 1.105.

**Table 1.105:** Causes of pulmonary oedema

**1. Cardiogenic**

- Left heart failure (e.g. mitral and aortic valve disease, HT)
- Acute MI
- Cardiac arrhythmias
- Acute pulmonary thromboembolism

**2. Noncardiogenic**

- Severe sepsis
- Inhalation of toxic and irritant gases (phosgene, phosphine (PH<sub>3</sub>), hyperbaric O<sub>2</sub>)
- High altitude pulmonary oedema
- Drowning or near drowning
- Aspiration of gastric contents or corrosive poisoning
- Aluminium phosphide poisoning (insecticide, pesticide)
- Acute haemorrhagic pancreatitis
- Narcotic overdose
- Snake bite
- Acute fulminant hepatitis (hepatic failure)
- Sudden removal of air (pneumothorax) or fluid (pleural effusion) from thoracic cavity
- Fluid overload
- Chronic renal failure (CRF), Goodpasture's syndrome

## CASE 30: MITRAL REGURGITATION

The patient (not shown) presented with complaints of palpitation, dyspnoea, PND and chest discomfort. There was history of cough with no haemoptysis. Patient has history of pain abdomen and oedema feet.

Examination revealed normal pulse, BP, IVP. Apex beat was down and outside the midclavicular line in 5th intercostal space, forceful and diffuse. Left parasternal heave present. A systolic thrill present at apex. The auscultatory findings included soft and muffled  $S_1$ , a pansystolic murmur, a third heart sound (Fig. 1.30).

## History–Points to be asked/noted

Ask for the followings;

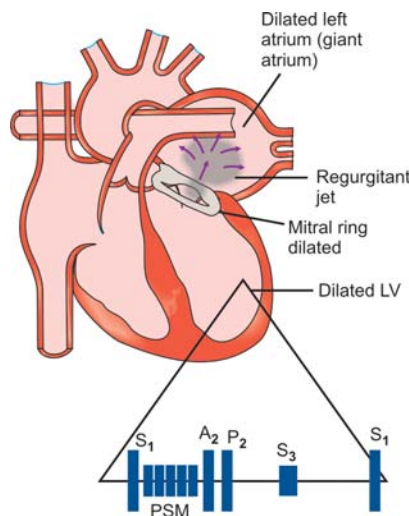
- Exertional dyspnoea, nocturnal dyspnoea, palpitation
- Symptoms of acute pulmonary oedema, e.g. cough, frothy sputum, dyspnoea at rest and haemoptysis
- Fatigue, weakness, tiredness due to reduced cardiac output.
- Puffiness of face, ankle or leg swelling, ascites due to right heart failure.
- History of trauma to chest or cardiac surgery.

## Past History

- Ask for history of sore throat, skin infection, rheumatic fever (joint pain)
- History of recurrent chest infections, fever, paralysis

## Signs

- Pulse may be good volume or normal volume. It is usually regular but becomes irregular in presence of atrial fibrillation or ventricular ectopics.
- Pulse pressure may be wide or normal. Note BP, temperature and respiration.
- Cyanosis (peripheral or central or both) may be present.
- Raised jugular venous pressure with prominent 'a' wave in severe pulmonary hypertension and 'v' wave if TR develops
- Pitting pedal oedema
- Look for signs of bacterial endocarditis, e.g. fever, splinter haemorrhage, Janeway's lesion, palmar erythema, clubbing of fingers, painful fingertips or gangrenous finger(s), cold extremities, red colouration of urine



**Fig. 1.30: Mitral regurgitation. Hemodynamic effects and auscultatory findings**

## Clinical Presentations

- The patient may be entirely asymptomatic, murmur is often detected in medical board examination more often in young females without any apparent disability
- These patients may present with symptoms of left heart failure (cough, dyspnoea, PND, haemoptysis, etc.)
- These patient in addition to above symptoms may present with complications, e.g. hemiplegia, gangrene of finger, toes
- Acute mitral regurgitation may present as acute LHF in a patient with acute MI due to rupture of papillary muscle or chordae tendinae

## Systemic Examination

## Inspection

- Apex beat is displaced down beyond 5th intercostal space outside the midclavicular line and is diffuse but forceful.
- Pulmonary artery pulsations in 2nd left intercostal space may be seen.
- Left parasternal left/heave may be visible.

## Palpation

- Left parasternal heave may be palpable.
- Displaced down and out forceful apex beat.
- Systolic thrill at apex may be palpable.
- $P_2$  may be palpable in pulmonary area in pulmonary hypertension

## Percussion

- Left border of heart corresponds to apex beat, i.e. dullness does not extend beyond apex beat.

## Auscultation

- First heart sound soft or muffled and buried in the pansystolic murmur
- Pansystolic murmur at apex, high-pitched soft and radiates to left axilla, heard with diaphragm of the stethoscope in expiration
- Third heart sound ( $S_3$ ) may be present, is caused by rapid flow of blood causing tensing of papillary muscle, chordae tendine and valve leaflets.
- $P_2$  may be loud and narrowly split. Ejection systolic and/or diastolic murmur (Graham-Steell) at 2nd left space. These are signs of pulmonary arterial hypertension.

## Examination of other systems

1. Respiratory system
  - Tachypnoea may be present
  - Crackles and rales at bases of lungs
2. Abdominal examination
  - Mild tender hepatomegaly
  - No ascites, no splenomegaly.

- Look for signs of acute rheumatic activity, e.g. arthritis, fever, erythema marginatum, subcutaneous nodules, etc.
- Note for the presence of features of Marfan's syndrome, e.g. tall stature arachnoidactyly, high-arched palate, ectopia lentis.

### 396. What is the clinical diagnosis in this case?

**Ans.** The symptoms and signs suggest the diagnosis of mitral regurgitation (MR) in this case.

### 397. How do you define mitral regurgitation? What are its haemodynamic consequences?

**Ans.** Regurgitation of blood through the mitral valve during systole is called *mitral regurgitation*.

#### Haemodynamic Consequences

Normally mitral valve closes during ventricular systole, but in mitral regurgitation, a small volume of blood regurgitates back into left atrium during systole in addition to left ventricular ejection into the aorta, leading to left atrial enlargement due to volume overload. During diastole, a large volume of blood from overloaded left atrium rushes to the left ventricle producing its subsequent enlargement, hence, the consequences of MR are:

- Dilatation of left atrium (*giant atrium*). It occurs first of all.
- Dilatation of left ventricle due to volume overload leading to subsequent LVF.
- The back flow of blood from overloaded left atrium produces lung congestion, pulmonary oedema and subsequent pulmonary arterial hypertension.
- Ultimately pulmonary arterial hypertension leads to right ventricular hypertrophy, then its failure leading to congestion of various viscera called congestive heart failure.

### 398. What are the causes of mitral regurgitation?

**Ans.** The mitral regurgitation occurs commonly from the dilatation of the mitral ring in rheumatic heart disease or due to diseases of myocardium and endocardium producing insufficient closure of the valve, though structurally valve may be normal. It may be either due to papillary muscle dysfunction or chordae tendinae rupture in patients with MI. The causes are given in Table 1.106.

**Table 1.106:** Causes of mitral regurgitation

1. Rheumatic (less common)
  - Rheumatic heart disease, acute rheumatic fever
2. Non-rheumatic (common)
  - Mitral valve prolapse
  - Myocarditis
  - Acute MI (due to papillary muscle dysfunction or rupture of chordae tendinae producing acute mitral regurgitation)
  - Infective endocarditis
  - Dilated cardiomyopathy
  - Trauma during valvotomy
  - Marfan's syndrome
  - SLE (Libman-Sack's endocarditis)
  - Rarely congenital
3. Left ventricular dilatation (volving dilatation)
 

Secondary to;

  - Aortic valve disease, e.g. AS, AR or both
  - Systemic hypertension

Note: Isolated mitral regurgitation is commonly non-rheumatic in origin.

### 399. Where are characteristics of severe MR?

**Ans.** Characteristic features of severe MR are as follows:

- i. *General physical signs*
  - A good volume pulse with wide pulse pressure
  - Raised JVP with prominent 'a' wave due to severe pulmonary hypertension, and a prominent 'v' wave if there is associated TR
  - Bilateral pitting pedal oedema
- ii. *Signs of left ventricular hypertrophy/failure*
  - Apex beat is hyperdynamic and goes down and out. A systolic thrill may be palpable.
- iii. *Signs of RVH*
  - Left parasternal heave
  - Epigastric pulsation
  - Signs of severe pulmonary hypertension (Read signs of pulmonary hypertension in MS).
- iv. *Auscultatory signs of mitral regurgitation*
  - The S<sub>1</sub> is generally muffled, soft or buried within pansystolic murmur
  - A pansystolic murmur radiating to left axilla



- $S_3$  may be audible due to rapid filling of left ventricle
- A short-soft diastolic murmur even in the absence of MS (functional MS) may be heard
- An  $S_4$  is audible in acute severe MR
- An OS may be heard in the absence of MS. Usually OS indicates associated MS but can be heard in severe MR.

#### Electrocardiogram

- P mitral, P- pulmonale or bifid P wave of biatrial enlargement with severe LVH.
- Atrial fibrillation common

*Colour Doppler* is the most accurate noninvasive technique for detection and estimation of severe MR.

#### 400. What is pansystolic murmur and what are its causes?

**Ans.** Pansystolic murmur is described as follows:

#### Definition

A pansystolic or holosystolic murmur starts with the first heart sound ( $S_1$ ) and continues throughout the systole and embraces  $S_2$ . It has uniform intensity hence called holosystolic.

#### Mechanism

As the left ventricle in MR is overloaded, its pressure exceeds LA pressure just after the first heart sound, hence, the regurgitant jet of blood starts flowing from LV to LA producing systolic murmur that continues throughout systole up to  $S_2$  until LA pressure exceeds the LV pressure to stop the jet.

#### Causes

1. MR due to any cause (read the causes in the Table 1.118).
2. TR. The pansystolic murmur is best audible in the tricuspid area (left parasternal), increases in intensity with inspiration (*Carvallo's sign*) and does not radiate to axilla. There may be prominent 'v' waves in JVP and liver may be pulsatile.
3. *Ventricular septal defect (mala de Roger)*. The murmur is rough, pansystolic, best heard across the

chest (on both sides of sternum). Very often, there is an associated thrill.

4. *Functional murmur*. These murmurs are usually soft, mostly midsystolic, may be pansystolic and do not radiate to the axilla. No change with posture and respiration.

#### 401. What does mid-diastolic murmur in MR indicate?

**Ans.** It indicates the followings:

1. Associated MS (i.e. MR with MS)
2. Severe MR with functional MS

#### 402. What are causes of acute MR?

**Ans.** Causes of acute MR are:

- Acute myocardial infarction with either rupture of papillary muscle or chordae tendinae.
- Subacute or acute bacterial endocarditis with rupture of valve cusps or chordae tendinae.
- Traumatic rupture of chordae tendinae.

#### 403. What are characteristics of mitral valve prolapse syndrome (Barlow's syndrome, midsystolic click-murmur syndrome, floppy mitral valve syndrome)?

**Ans.** The characteristic features of mitral valve prolapse (MVP) are:

- This is myxomatous degeneration of the mitral leaflets resulting in redundant mitral leaflets that prolapse into LA during systole.
- It is commonly seen in young females.
- It is asymptomatic and mid-systolic murmur or the click or both may be the only evidence.
- The prolapse of the posterior cusp (common) radiates the murmur towards right side while that of anterior cusp radiates the murmur to left axilla.
- It is commonly associated with ventricular arrhythmias, hence,  $\beta$ -blockers are indicated for symptom relief and prophylaxis.

#### 404. What the causes of mitral valve prolapse?

**Ans.** Following are causes:

- Marfan's syndrome
- Ehlers-Danlos syndrome
- Collagen vascular disorders (genetically determined)



- Straight-back syndrome (a thoracic cage abnormality)
- As a sequel of acute rheumatic fever
- Ischaemic heart disease
- Cardiomyopathy.

#### 405. What is Cooing or 'Sea guill' murmur?

**Ans.** When a patient of MR either develops SABE or rupture of chordae tendinae, a systolic murmur appears that has either a cooing or sea guill quality – here the chordae tendinae act like strings of a musical instrument. This type of murmur is also found in acute myocardial infarction with rupture of chordae tendinae and rarely in acute rheumatic carditis.

#### 406. What is effect of Valsalva manoeuvre on MR?

**Ans.** The systolic murmur of MR is increased by isometric strain (hand – grip) but is reduced during the Valsalva manoeuvre.

#### 407. What are clinical signs of congestive heart failure?

**Ans.** Following are signs of congestive heart failure:

- Extremities may be cold or pale.
- Tachycardia and tachypnoea.
- Profuse sweating or perspiration.
- Central cyanosis.
- Low volume pulse or pulsus alternans.
- Cheyne – Stokes breathing.
- Third heart sound ( $S_3$ ). Ventricular gallop rhythm means triple rhythm ( $S_1$ ,  $S_2$ ,  $S_3$  sounds) with tachycardia – is so named because it resembles with the cadence produced by galloping of a horse).
- Fine basal pulmonary rales / crackles.
- Expiratory wheezing.
- Hydrothorax or pleural effusion.
- Oliguria and nocturia.
- Cardiomegaly with other signs of basic heart disease (For signs of basic heart disease, one should read the specific disorder).

#### 408. How will you arrive at the diagnosis of congestive heart failure (CHF)?

**Ans.** The diagnosis of CHF is based on presence of some combinations of the clinical manifestations described in Table 1.107, together with the findings characteristics of one of the underlying forms of heart disease.

**Table 1.107:** Framingham criteria for diagnosis of CHF

##### Major criteria

- Paroxysmal nocturnal dyspnoea (PND)
- Distended neck veins
- Cardiomegaly
- Rales
- Acute pulmonary oedema
- $S_3$  gallop
- Increased venous pressure ( $>16$  cm  $H_2O$ )
- Positive hepatojugular reflux

##### Minor criteria

- Peripheral pitting oedema
- Night cough
- Dyspnoea on exertion
- Hepatomegaly
- Pleural effusion (hydrothorax)
- Reduced vital capacity by 1/3 of normal
- Tachycardia ( $\geq 120$  bpm)

NB: To establish the diagnosis of CHF, at least one major and two minor criteria are required

#### 409. What are the causes of right heart failure?

**Ans.** Following are the causes:

##### 1. Pulmonary valve disease

- Pulmonary stenosis
- Pulmonary hypertension due to any cause
- Acute cor pulmonale (pulmonary thrombo-embolism)
- Chronic cor pulmonale

##### 2. Tricuspid diseases

- Tricuspid stenosis
- Tricuspid regurgitation (dilated cardiomyopathy)
- Ebstein anomaly

##### 3. Depressed myocardial contractility

- Right ventricular infarction
- Right ventricular dysplasia (right ventricular cardiomyopathy)
- Myocarditis

**4. Secondary to left heart failure.** The left ventricular failure ultimately may lead to right ventricular failure.

#### 410. What are the complications of MR?

**Ans.** Complications of MR are:

- Acute LVF (acute pulmonary oedema). It is characterised by persistent coughing with bringing out of small amount of frothy pink coloured sputum with increasing breathlessness, orthopnoea, PND,

tachypnoea, tachycardia and central cyanosis. The chest shows diffuse bilateral crackles and rales throughout both lungs. The X-ray is diagnostic.

- Infective endocarditis.
- CHF and deep vein thrombosis.
- Arrhythmias, e.g. ventricular ectopics, atrial fibrillation common. Atrial fibrillation is due to giant left atrium.
- Giant left atrium may produce pressure symptoms, e.g. hoarseness, dysphagia.

#### **411. How will you investigate a patient with MR?**

**Ans.** Investigations required are as follows:

##### **1. Chest X-ray.** It may show;

- Cardiac shadow is enlarged and occupies >50% of transthoracic diameter.
- The left atrium may be massively enlarged and forms the right border of the heart.
- The left ventricle is also enlarged producing *boot-shaped heart*.
- There may be pulmonary venous congestion (e.g. upper lobar veins prominent producing increased bronchovascular marking or there may be diffuse haze from hilum to periphery – pulmonary oedema), interstitial oedema (*Kerley's B lines*) and sometimes interlobar fissure effusion or hydrothorax.
- Mitral valve calcification may occur, seen in penetrating films.

##### **2. ECG.** It may show;

- Right atrial, left atrial or biatrial hypertrophy
- LV or biventricular hypertrophy
- AF

**3. Echocardiogram and Doppler imaging.** The 2.D-echocardiogram is useful for assessing the cause of MR and for estimating the LV function and ejection fractions. Left atrium is enlarged. Vegetations may be seen in infective endocarditis. The echocardiogram shows characteristic feature of MVPS (incomplete coaptation of anterior and posterior leaflets).

**4. Colour Doppler flow study** is most accurate diagnostic technique for detection and quantification of MR.

#### **412. What are the cause of LVH? What are its ECG characteristics?**

**Ans.** Reas section on ECG or read Practical Electrocardiography by Dr SN Chugh.

#### **413. How will you treat a patient with MR?**

**Ans.** Treatment consists of symptomatic relief to be provided by medical treatment and permanent relief by surgical treatment (valve replacement).

##### **1. Medical treatment**

- Salt restriction
- Digitalis and diuretics
- Bronchodilatation if there is severe bronchospasm
- Vasodilators (ACE-inhibitors) to reduce the regurgitant flow in severe cases.
- **Prophylaxis.** Penicillin prophylaxis is must.

##### **2. Surgical treatment is valve replacement**

#### **414. How will you decide clinically the dominance of mitral valve lesion in a patient with combined mitral valve disease (MS and MR)?**

**Ans.** The dominance is decided by features described in Table 1.108.

#### **415. What are signs of digitalis toxicity?**

**Ans.** The signs are as follows:

1. *GI manifestations*, e.g. anorexia, nausea, vomiting. These are earliest to appear.
2. *Cardiac arrhythmias and conduction disturbances*
  - Premature ventricular complexes (VPCs) usually ventricular bigeminy or multiforme.
  - Nonparoxysmal atrial tachycardia with block
  - Varying degrees of AV block
  - Sinoatrial block (SA block)
  - Ventricular tachycardia; bidirectional ventricular tachycardia is mainly due to digitalis
  - Ventricular fibrillation
3. *Miscellaneous effects*
  - Weight loss
  - Cardiac cachexia
  - Gynaecomastia
  - Yellow vision (xanthopsia)
  - Mental features, e.g. agitation

**Table 1.108:** Features of dominant MS or MR in combined valvular lesion

Feature	Dominant MS	Dominant MR
<b>1. Clinical presentations</b>	Dyspnoea on exertion orthopnoea and PND. Palpitation is uncommon occurs if AF present	Palpitations common, followed by dyspnoea, orthopnoea and PND
<b>2. Symptoms</b>		
• Haemoptysis and PND	Marked	Mild
• Symptoms of CHF		
• Systemic embolisation		
• Lung congestion		
<b>3. Signs</b>		
Pulse	Low volume	Normal volume
BP	Low systolic	Within normal limits
Apex	Tapping	Heaving
Left parasternal heave	Grade III	Grade I
First heart sound	Short, loud and snappy	Soft or muffled
Opening snap	Present	Absent
Third heart sound (S <sub>3</sub> )	Absent	Present
Murmur and thrill	<ul style="list-style-type: none"> <li>Rough and rumbling diastolic murmur with thrill</li> <li>Pansystolic murmur present, does not radiate to axilla</li> </ul>	<ul style="list-style-type: none"> <li>Soft pansystolic murmur radiating to axilla with a systolic thrill</li> <li>Soft mid-diastolic murmur</li> </ul>
Chest X-ray	Mitralised heart	Cardiomegaly with giant left atrium forming right heart border
ECG	RVH with left axis deviation	LVH with right axis deviation

**416. How will you treat digitalis toxicity?**

**Ans.** The steps of treatment are:

- Stop digoxin
- Stop diuretic
- Give potassium
- Give phenytoin for digitalis-induced arrhythmias
- Give digitalis Fab antibody

**417. Mention recent Jones Criteria for acute rheumatic fever.**

**Ans.** Table 1.109 explains the Jones's criteria for acute rheumatic fever.

**Table 1.109:** Jones's diagnostic criteria for acute rheumatic fever**1. Major**

- Carditis
- Polyarthritides
- Chorea
- Erythema marginatum
- Subcutaneous nodules

**2. Minor**

- Fever
- Arthralgia
- Previous rheumatic fever
- Raised ESR or C-reactive protein
- Leucocytosis
- First degree or second degree AV block

The diagnosis is *definite* if;

- Two or more major manifestations are present, or
  - One major and two or more minor manifestations
- Plus*
- Supporting evidence of preceding streptococcal infection, recent scarlet fever, raised ASO titres or other streptococcal antibody titre, positive throat culture, or echocardiographic evidence of carditis.

## CASE 31: INFECTIVE ENDOCARDITIS

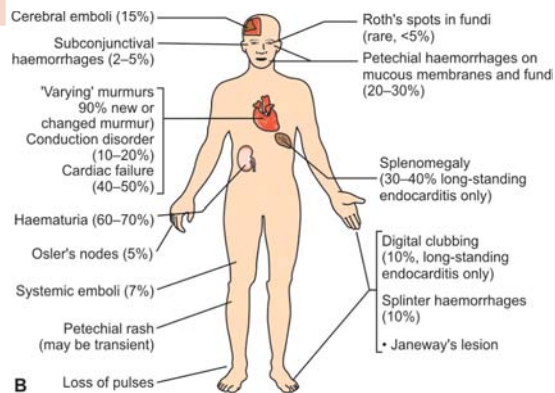
The patient presented with palpitation, cough, breathlessness and chest discomfort. There was history of PND and oedema of feet off and on for the last few years. He was taking treatment and oedema and breathlessness relieved. Now he complained of fever with chills, rigors and diaphoresis. He developed gangrene of the fingers (Fig. 1.31A) suddenly

## History—Points to be Noted

- Dyspnoea, palpitation, cough, chest discomfort due to basic heart disease, i.e. valvular or congenital lesion
- Fever with chills, diaphoresis
- Symptoms of complications such as CHF or systemic embolisation e.g. cold extremity, hemiplegia, haematuria
- Visual disturbance or visual loss
- Onset, duration of symptoms.
- History of fever, sore throat
- History of procedure or dental extraction in a patient with underlying congenital or acquired valvular heart disease
- History of recent cardiac surgery
- History of I.V. drug misuse
- History of sepsis, skin infection
- Ask about Past history of rheumatic or congenital heart disease

## General Physical Examination

- General look-toxic. Patient is febrile
- Weight loss
- The skin may show purpuric spot, ecchymosis, Janeway lesion
- Neck for JVP and lymphadenopathy
- **Extremities.** Look for coldness
  - Clubbing of fingers
  - Digital gangrene
  - Splinter haemorrhage
  - Osler's nodes
  - Painful finger tips
- Eyes for subconjunctival haemorrhage, Roth's spots
- Look for anaemia, cyanosis, jaundice, oedema
- Examine vitals, e.g. pulse, BP, respiration and temperature



**Figs 1.31A and B: Infective-endocarditis**  
 A. Gangrenous fingers, hand and forearm on left side due to embolic occlusion of brachial artery on Doppler study. The patient had cold extremities with absent brachial and radial pulses on left side. B. Clinical features of endocarditis

## Systemic Examination

1. CVS
  - Inspection
  - Palpation
  - Percussion
  - Auscultation
2. Other systems
  - Nervous system for motor or sensory deficit due to embolisation. Examine ocular fundi
  - Respiratory system for pulmonary embolism, infection, LVF
  - Kidneys for pain and tenderness in renal area or haematuria.
  - Palpate for splenomegaly and hepatomegaly

## Clinical Presentations

1. **Acute infective endocarditis** caused by more virulent organisms mostly *staphylococcus aureus* involves normal heart valves or cardiac structures, produces acute fibrile illness with fever, chills, diaphoresis and acute onset of regurgitant murmur due to damage to valves and cardiac structures, with septic embolisation to various viscera and peripheral structures.
2. **Subacute infective endocarditis** caused by less virulent organisms such as bacteria i.e. (Streptococci, pneumococci, Staphylococci, fastidious gram-negative coccobacilli, HACEK group- Hemophilus, Actinobaccillus, Cardiobacterium, Eikenella and Kingella), fungi (candida) or rickettsia cause insidious onset of fever with chills and rigors, changing or new cardiac murmurs, precipitation of CHF and embolisation to viscera and peripheral structures in a patient who is already suffering from either a congenital heart disease or acquired rheumatic heart disease or has undergone cardiac surgery or has prosthetic valve.

**418. What is your clinical diagnosis?**

**Ans.** In view of history suggestive of some heart disease with CHF combined with embolic occlusion of brachial artery with gangrenous fingers, the provisional diagnosis is infective endocarditis due to underlying cardiac disorder which will be apparent on physical signs and on investigations.

**419. How you do define endocarditis?**

**Ans.** Infective endocarditis is due to microbial infection of a heart valve (native, prosthetic), the lining of a cardiac chamber, or blood vessels or a congenital septal defect or a congenital anomaly. The causative organism is either a bacterium or a fungus or a rickettsia (Q fever endocarditis or chlamydia).

*Acute endocarditis* is usually bacterial in origin, has rapid onset, fulminant course causing destruction of cardiac structures, perforation of valve cusps and

hematogenously seeds the extracardiac sites, and if untreated, progresses to death within weeks.

*Subacute endocarditis* follows an indolent course, causes structural cardiac damage slowly and rarely causes metastatic infection, and is gradually progressive unless complicated by a major embolic event or rupture of mycotic aneurysm.

**420. What are symptoms and signs of endocarditis? What is their pathogenesis?**

**Ans.** The symptoms and signs (Table 1.110) are due to

- Infection and fluctuating toxemia
- Embolisation
- Immune-complex mechanism
- Anaemia

**421. What are complications of endocarditis?**

**Ans.** Common complications are:

1. *Heart failure.* Endocarditis may precipitate or

**Table 1.110:** The symptoms and signs of infective endocarditis

Organ	Symptoms	Signs (Fig. 1.31B)
General	Fever, nausea, anorexia, sweating, weakness	Temperature is raised, weight loss is present
Heart	Dyspnoea, palpitations, cough, pain chest	<ul style="list-style-type: none"> <li>• Tachycardia</li> <li>• Changing or appearance of new murmurs</li> <li>• Conduction defects</li> <li>• CHF</li> <li>• Muffling of heart sounds</li> </ul>
Lung	Haemoptysis, chest pain	Pleuritic rub due to embolic pulmonary infarct may be present
CNS	Headache, toxic encephalopathy, meningitis	Monoplegia or hemiplegia due to embolisation
Blood vessels	Coldness of extremities	<ul style="list-style-type: none"> <li>• Loss of peripheral pulses due to embolisation</li> </ul>
Hands		<ul style="list-style-type: none"> <li>• Digital gangrene</li> <li>• Clubbing of the fingers</li> <li>• Splinter haemorrhages</li> <li>• Osler's nodes (painful tender swellings at fingertips)</li> <li>• Janeway's lesion (large nontender maculopapular eruptions in palm and sole)</li> </ul>
Skin		<ul style="list-style-type: none"> <li>• Petechial haemorrhage</li> <li>• Purpuric spots</li> </ul>
Eyes	Redness of eyes, visual disturbance, sudden blindness	<ul style="list-style-type: none"> <li>• Subconjunctival hemorrhage</li> <li>• Roth's spots</li> </ul>
Kidneys	<ul style="list-style-type: none"> <li>• Haematuria</li> <li>• Acute flank pain</li> </ul>	<ul style="list-style-type: none"> <li>• Renal angle tender</li> </ul>
Spleen	Pain in splenic area	<ul style="list-style-type: none"> <li>• Splenomegaly</li> <li>• Splenic infarct (rub)</li> </ul>
Blood	Pallor, lassitude, fatigue	<ul style="list-style-type: none"> <li>• Anaemia</li> </ul>



aggravate the heart failure which may occur following a tear in a leaflet, ruptured chordae tendinae, dehiscence of a prosthetic valve or perforation of interventricular septum

2. *Embolisation* to any organ producing an infarct
3. *Neurological complications*. Embolic stroke is the most common neurological complication. Intracranial haemorrhage may occur due to ruptured mycotic aneurysm or rupture of an artery due to septic arteritis. Meningitis and brain abscess can occur.
4. Septicaemia.

#### 422. What are clinical features of acute bacterial endocarditis?

**Ans.** Clinical features are as follows:

- Often involves the normal heart valves and has rapid downhill course.
- *Staphylococcus* is the commonest pathogen
- Right sided involvement is common because it is common in I.V. drug users. Pneumonia is common.
- Clubbing is not a feature.
- Source of infection is evident, i.e. Staphylococcal abscess or pneumococcal meningitis.
- Cardiac and renal failure develop rapidly.
- Perforation of cusps (aortic, mitral) may occur leading to acute valvular regurgitation.

#### 423. What is right sided endocarditis?

**Ans.** Main features are as follows:

- Commonly caused by *S. aureus*.
- Tricuspid valve is commonly affected producing regurgitation. Pulmonary valve involvement is rare.
- Involvement of right ventricular wall is common in VSD.
- Common in drug addicts using I.V line for drug delivery. It may occur in immunocompromised patients and those with burns
- Prognosis is better
- Systemic embolisation is rare. Lung infarction or pulmonary infection (lung abscess, empyema, pneumonias) are common.

#### 424. When do you suspect infective endocarditis in a patient with heart lesion?

**Ans.** Diagnosis of infective endocarditis is suspected in each and every patient of rheumatic valvular heart

disease or a congenital heart disease developing fever, tachycardia, worsening dyspnoea or congestive heart failure or an embolic episode, e.g. monoplegia/hemiplegia, haematuria, etc.

The clinical supportive features include:

- Fever (swinging temperature)
- Pallor, anaemia, toxic look, tachypnoea and tachycardia
- Clubbing of the fingers
- Splenomegaly (mild)
- Microscopic haematuria
- Embolic manifestations

#### 425. Name the predisposing factors for endocarditis.

**Ans.** Predisposing factors are:

1. *Valvular heart disease*. Mitral and aortic valvular lesion predispose to infective endocarditis. Regurgitant lesions are more prone to produce endocarditis as the regurgitant jet damages the mural endocardium and predisposes to seeding of the organism. The mitral valve involvement is commoner than aortic. The tricuspid valve is involved in right sided endocarditis. Pulmonary valve is rarely involved.
2. *Congenital heart disease*. The VSD, PDA and bicuspid aortic valve are common predisposing lesions. It occurs on low pressure side of the ventricular septum i.e. on right ventricular endocardium in VSD. The ASD does not lead to endocarditis.
3. *Prosthetic valve or a foreign body* also predispose to endocarditis.
4. *Immunocompromised state* either due to disease (diabetes, malignancy) or due to drugs (steroids and immunosuppressive drugs) predispose to it. In such patients acute bacterial endocarditis is common.
5. *Intravenous drug abusers*
6. *Prior heart surgery* (valvotomy, balloon dilatation and valve replacement).

#### 426. How will you investigate a patient suspected of endocarditis?

**Ans.** Investigations required are as follows:

1. *Blood examination*. There may be anaemia (normocytic normochromic) leucocytosis and raised ESR and high C-reactive protein levels
2. *Urine examination* reveals mild albuminuria and microscopic haematuria. Gross haematuria is rare

3. *Immune- complex titre and rheumatoid factor titres* may be elevated
4. *Blood culture.* Isolation of the micro-organism from blood cultures is crucial not only for diagnosis but also for determination of antimicrobial sensitivity and planning the management. In the absence of prior antibiotic therapy; a total of 3 blood culture sets, ideally with the first separated from the last by at least 1 hour should be obtained from different venipuncture sites over 24 hour. If the cultures remain negative after 48 to 72 hours; two or three additional blood culture, including a lysis–centrifugation culture, should be obtained, and the laboratory should be asked to pursue fastidious microorganisms by prolonging the incubation time and performing special subcultures.  
It is likely that 95-100% of all cultures obtained will be positive and that one of the first two cultures will be positive in at least 98% of patients. Blood culture obtained just prior to temperature peak will give a higher yield. Blood culture is likely to be sterile if patient has already received antibiotic.
5. *Echocardiogram.* Vegetations may be identified as small, sessile or polypoidal masses on heart valves or congenital defects. Transthoracic echocardiography is noninvasive and exceptionally specific, but has sensitivity of 65%. Transoesophageal echocardiography offers the greatest sensitivity for detection of vegetations.
6. *Serological tests.* Serological tests including polymerase chain reaction can be used to identify some organisms that are difficult to recover from the blood culture.

#### 427. What are the diagnostic criteria for endocarditis?

**Ans.** The diagnosis of infective endocarditis is established with certainty only if culture from the vegetations is positive. Nevertheless, a highly sensitive and specific diagnostic criteria – Duke’s criteria has been developed on the basis of clinical, laboratory and echocardiographic findings (Table 1.111).

**Table 1.111:** The Duke criteria for the clinical diagnosis of infective endocarditis

#### **Infective endocarditis is definite if following criteria using specific definitions listed below are met;**

Two major criteria **or**

One major and three minor criteria **or**

Five minor criteria

##### *Major criteria*

##### 1. *Positive blood culture*

- i. Typical microorganism for infective endocarditis from two separate blood cultures
  - Viridans streptococci, *Streptococcus bovis*, HACEK group, *Staphylococcus aureus* **or** Community-acquired enterococci in the absence of a primary focus, **or**
- ii. Persistently positive blood culture, defined as recovery of a microorganism consistent with infective endocarditis from:
  - Blood cultures drawn >12 hour apart; **or**
  - All of three or a majority of four or more separate blood cultures, with first and last drawn at least 1 hour apart
  - Single positive blood culture for *Coxiella burnetii* or phase 1 IgG antibody titer of >1:800

##### 2. *Evidence of endocardial involvement*

- Positive echocardiogram, i.e. Oscillating intracardiac mass on a valve or supporting structures or in the path of regurgitant jet or in implanted material, in the absence of an alternative anatomic explanation, **or**
- Abscess, **or**
- New partial dehiscence of prosthetic valve, **or**
- New valvular regurgitation (increase or change in preexisting murmur not sufficient)

##### *Minor criteria*

1. *Predisposition:* predisposing heart condition or injection drug use
2. *Fever* = 38°C (=100.4°F)
3. *Vascular phenomena:* major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracardial haemorrhage, conjunctival haemorrhage, Janeway lesions
4. *Immunologic phenomena:* glomerulonephritis, Osler’s nodes, Roth’s spots, rheumatoid factor
5. *Microbiologic evidence:* positive blood culture but not meeting major criterion as noted previously for serologic evidence of active infection with organism consistent with infective endocarditis
  - Excluding single positive culture for coagulase-negative staphylococci and diphtheroids, which are common culture contaminants, and organisms that do not cause endocarditis frequently, such as gram-negative bacilli

*Abbrev:* HACEK, Hemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella.

## CASE 32: COR PULMONALE

A-60-year male (Fig. 1.32A) presented with cough, breathlessness, progressive in nature for the last 7 years. He has been taking treatment and getting relief on and off. Now for the last 1 month, he complains of increase in breathlessness, cough and oedema of legs and feet.

## History–Points to be noted

Ask about;

- Cough, its frequency, seasonal relation, nocturnal etc.
- Sputum production, quantity, colour, smell, consistency and history of haemoptysis
- Any recent change in the symptoms. History of recent fever, sore throat or loose motions
- History of swelling feet, abdomen (hepatomegaly)
- Ask for any aggravating or relieving factors
- Take full drug history, drug being taken and their effect

Past history

- Cough or expectoration in the past
- History of allergy or rhinitis or asthma in the past

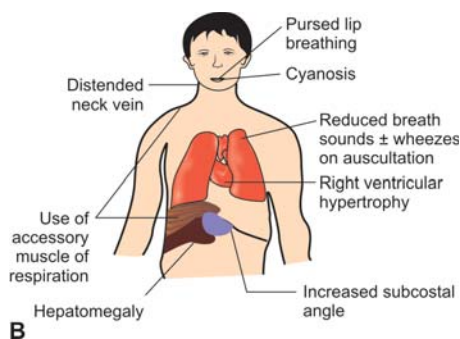
Personal history

- History of smoking, alcoholism, exposure to dust or fumes

Occupational history

## General Physical Examination

- Patient is orthopnoic, sitting with hands on cardiac table or legs dangling/hanging from the bed to relieve breathlessness
- Cyanosis present
- Neck veins distended. JVP raised. There may be v and y collapse due to TR.
- Pulse and respiratory rate increased
- Warm extremities, clubbing of fingers and oedema feet may be present
- Purse-lip breathing may be present
- Action of extra-respiratory muscles, i.e. there may be hyperactivity



**Figs 1.32A and B:** A. Chronic cor pulmonale. The patient has signs of COPD. Note the purse lip breathing, cyanotic spells. The patient has oedema and raised JVP. Note the common position adopted by patient with COPD and acute exacerbation with cor pulmonale to get relief from breathlessness. B. Clinical signs of chronic cor pulmonale (diagram).

## Clinical Presentation

- Patients suffering from chronic lung disease (obstructive or suppurative or interstitial) present with signs of right ventricular failure (distended neck veins, cyanosis, tender hepatomegaly and pitting edema).
- A patient with chronic chest deformity, e.g. kyphoscoliosis may present with symptoms of progressive dyspnoea, worsening cough over the last few years. They may complain of pain abdomen and oedema feet due to right heart failure.

## Systemic Examination

## 1. Examination of respiratory system

- Inspection
  - Palpation
  - Percussion
  - Auscultation
- There will be evidence of COPD or other chronic lung disease

## 2. Examination of CVS

Inspection

- Apex beat may be normally placed or centrally placed or displaced outwards but not downwards or may not be visible
- No other visible pulsation

Palpation

- Apex beat may be palpable outside the midclavicular line
- Parasternal heave present
- Right ventricular pulsations palpable in epigastrium

Percussion

- Cardiac dullness may be masked or just limited to centre

Auscultation

- Heart sounds normal
- Second heart sound narrowly split
- There may be an ejection systolic murmur in  $P_2$  area and a pansystolic murmur in tricuspid area

## 3. Abdominal examination

- Liver is enlarged, soft, tender and may be pulsatile if TR present
- There may signs of ascites.

**428. What is your clinical diagnosis?**

**Ans.** The symptoms and signs suggest COPD with chronic cor pulmonale without respiratory failure.

**429. How do you define cor pulmonale?**

**Ans.** *Chronic cor pulmonale* is defined as right ventricular hypertrophy or dilatation secondary to the disease of the lung parenchyma, pulmonary vasculature, thoracic cage and ventilatory control.

*Acute cor pulmonale* is defined clinically as acute right ventricular hypertrophy or dilatation secondary to acute pulmonary thromboembolism.

**430. What are the causes of chronic cor pulmonale?**

**Ans.** Chronic cor pulmonale is secondary to development of pulmonary arterial hypertension which may be primary (idiopathic) or secondary due to disease of pulmonary vasculature or pulmonary parenchyma or thoracic cage. The causes are described in Table 1.112.

**431. What are clinical features of chronic cor pulmonale due to COPD?**

**Ans.** The clinical signs (Fig. 1.32B) are divided into two parts;

1. **Clinical signs of COPD** (read case discussion on COPD). However, few important clinical signs are;
  - Pursed -lip breathing
  - Use of accessory muscles of respiration
  - Barrel-shape chest
  - Cyanosis
  - Restricted chest movements and expansion

**Table 1.112:** Causes of cor pulmonale

- |   |
|---|
| <ol style="list-style-type: none"> <li>1. <b>Hypoxic vasoconstriction</b> <ul style="list-style-type: none"> <li>• COPD, cystic fibrosis</li> <li>• Chronic hypoventilation               <ul style="list-style-type: none"> <li>• Obesity</li> <li>• Sleep apnoea</li> <li>• Neuromuscular disease</li> <li>• Chest wall dysfunction</li> <li>• Idiopathic</li> </ul> </li> </ul> </li> <li>2. <b>Occlusion of pulmonary vascular bed</b> <ul style="list-style-type: none"> <li>• Pulmonary thromboembolism</li> <li>• Primary pulmonary hypertension</li> <li>• Pulmonary angitis</li> <li>• Sickle cell disease</li> </ul> </li> <li>3. <b>Parenchymal lung disease</b> <ul style="list-style-type: none"> <li>• Hypertrophic emphysema</li> <li>• Diffuse bilateral bronchiectasis</li> <li>• Diffuse interstitial lung disease</li> </ul> </li> </ol> |
|---|

- Reduced palpable length of trachea
- Intercostal indrawing
- Vocal fremitus reduced
- Percussion note hyper-resonant, cardiac dullness and liver dullness masked
- Harsh vesicular breathing with prolonged expiration
- Crackles and rhonchi/rales.

2. **Clinical signs of pulmonary arterial hypertension (PH)** Here due to presence of COPD, some signs of PH will be masked such as pulsations of pulmonary artery in second left interspace and cardiac apex beat and dullness. The physical signs which will be present include.

**A. General physical**

- Pulse-low volume
- Neck veins – distended. JVP raised and ‘a’ wave prominent

**B. Signs on chest examination****Inspection**

- Epigastric pulsations due to RV hypertrophy
- Pulmonary artery pulsations in 2nd left interspace may not be visible due to hyperinflated lungs covering the artery

**Palpation**

- Apex beat may not be visible
- P<sub>2</sub> is palpable
- Left parasternal heave may be present due to RVH.

**Percussion**

- Cardiac dullness will be masked due to hyperinflated lungs or limited to centre (heart is pushed centrally by the overdistended lungs).

**Auscultation**

- Loud P<sub>2</sub> – an ejection click may be present
- Ejection systolic murmur
- Close or narrow splitting of S<sub>2</sub>
- Graham-Steell murmur
- Right sided S<sub>3</sub>.

**432. Does definition of cor pulmonale include right heart failure? What are its signs?**

**Ans.** Right heart failure is not included in the definition of chronic cor pulmonale. It is a complication of cor pulmonale.



## 152 Bedside Medicine

The signs of right ventricular failure are:

- Raised JVP/distended neck veins with v and y collapse
- Hepatojugular reflux will be positive
- Liver will be enlarged and tender, may be pulsatile if functional TR present
- A pansystolic murmur of TR, heard best in left parasternal edge or in epigastrium
- Pitting pedal oedema and/or ascites.

### 433. How do you classify pulmonary arterial hypertension?

**Ans.** See Table 1.113.

**Table 1.113:** Classification of pulmonary hypertension

- |   |
|---|
| <b>I. Primary pulmonary hypertension</b> <ul style="list-style-type: none"><li>• Idiopathic</li></ul>   |
| <b>II. Secondary pulmonary hypertension</b> <ul style="list-style-type: none"><li>• Passive or reactive (from left sided heart lesions) such as MS, MR, AS and AR</li><li>• Hyperkinetic (left to right shunt), e.g. ASD, VSD, PDA</li><li>• Vasoconstrictive (hypoxic) chronic cor pulmonale</li><li>• Obstructive (reduction in vascular bed), e.g. pulmonary thromboembolism (acute cor pulmonale)</li><li>• Obliterative, e.g.<ul style="list-style-type: none"><li>• Pulmonary angitis/vasculitis</li><li>• Sickle cell disease</li><li>• SLE, PAN, CREST syndrome</li></ul></li></ul> |

### 434. What is normal pulmonary arterial pressure? What is pressure in pulmonary hypertension?

**Ans.** Normal pulmonary arterial pressure 18-25/6-10 mmHg.

In pulmonary hypertension;

- Pulmonary artery systolic pressure is >30 mmHg
- Mean pulmonary artery wedge pressure is >20 mmHg

### 435. What are causes of TR? Name its two characteristics?

**Ans.** The causes of TR are given in the box:

#### Causes of TR

- |  |
|--|
| <ol style="list-style-type: none"><li>1. Right ventricular dilatation secondary to pulmonary hypertension</li><li>2. Rheumatic heart disease</li><li>3. Right sided endocarditis in drug abusers</li><li>4. Right ventricular infarction</li><li>5. Carcinoid syndrome</li></ol> |
|--|

The two characteristics signs of TR are:

1. Distended neck veins with typical 'V' and 'Y' collapse
2. Pulsatile liver.

### 436. How will you investigate a patient with cor pulmonale?

**Ans.** Investigations required are as follows:

1. *Chest X-ray.* It will show;
  - Cardiomegaly
  - Pulmonary conus is prominent
  - Hilar bronchovascular markings prominent with pruning of the peripheral pulmonary vessels
  - Signs of COPD (emphysema) on X-ray will be evident (read radiology section)
2. *ECG.* It will show
  - Low voltage graph
  - Right axis deviation, clockwise rotation
  - Right atrial hypertrophy (P- pulmonale)
  - Right ventricular hypertrophy ( $R>S$  or  $R:S >1$  in lead  $V_1$  but both complexes being small)
  - $S_I, S_{II},$  and  $S_{III}$  syndrome
  - ST-T wave changes
  - Arrhythmias (MAT—multifocal atrial tachycardia is common)
3. *Echocardiography* It will show right atrial and right ventricular enlargement. Interventricular septum is displaced leftward. Colour Doppler may reveal functional TR
4. *MRI* is useful to measure RV mass, wall thickness, and ejection fraction
5. *Ventilation and perfusion scan*
6. *Systemic venography* and Doppler study may reveal deep vein thrombosis
7. *Cardiac catheterisation* for measurement of pulmonary vascular pressures, calculation of pulmonary vascular resistance and response to vasodilator therapy.

### 437. What are the complications of cor pulmonale?

**Ans.** Following are complications:

- Right heart failure
- Secondary polycythemia
- Deep vein thrombosis
- Cardiac arrhythmias (multifocal atrial tachycardia, ventricular arrhythmias)



### CASE 33: HEMIPLEGIA

A young female (18 yrs-Fig. 1.33) presented with cough and breathless on exertion for the last 4 yrs. She was well on treatment. There was no history of orthopnoea, PND, haemoptysis or pain chest. Now for the last 2 days, she is complaining of weakness of right half of the body with deviation of face. After recovery, she was able to walk and the picture was taken to show the gait.

#### History—Points to be Noted

- Note the date and time of onset of stroke
- Mode of onset, e.g. sudden or gradual
- Evaluation of paralysis, i.e. whether it was TIA, stroke-in-evolution or completed stroke
- Any known precipitating factor(s)
- Progress or course of paralysis, e.g. improving, stationary or deteriorating or waxing and waning
- Any associated motor and sensory symptoms
- Any disturbance of consciousness/convulsion, visual disturbance, speech disturbance
- Symptoms of raised intracranial tension

#### Past History

- History of similar episodes in the past which recovered completely (TIA)
- History of head injury or epilepsy
- History of HT, diabetes, RHD, meningitis, tuberculosis, migraine, exposure to sexually transmitted diseases
- Intake of oral contraceptive.

**Family history,** e.g. HT, DM, Epilepsy, migraine and similar illness in other family members.

**Personal history.** History of overweight or obesity, smoking, alcoholism.



**Fig. 1.33:** A young female with hemiplegia walking with circumducting gait. She has recovered recently from stroke

#### Clinical Presentations

- Patient usually complain of weakness of one half of the body with asymmetry of face. There may be complaints of sensory and speech disturbance.
- In addition to weakness, patient may complain of symptoms of the underlying disorder if it is the cause, i.e. hypertension, diabetes, TIA, rheumatic heart disease (valvular lesion Fig. 1.33), cardiomyopathy, etc.

#### Examination

1. *General physical*
  - Is patient conscious or cooperative?
  - Posture of the patient
  - Neck examination for pulsations, lymph node, thyroid
  - Vitals, e.g. pulse, BP and temperature
  - Oedema
  - Any obvious deformity
2. *Nervous system (read proper nervous system examination)*
  - Higher functions
  - Cranial nerves (UMN or LMN paralysis of 7th nerve), fundus for papilloedema
  - Neck rigidity absent
  - *Motor system examination*
    - There will be UMN signs on the side of the body involved (i.e. opposite to the CNS lesion) if lesion is above the cervical cord
    - Gait will be spastic
    - Cerebellar and autonomic functions normal
    - Speech involved if dominant hemisphere is the site of lesion
  - Sensory system may show hemianaesthesia or may be normal
3. *Other systems examination*
  - CVS
  - Respiratory
  - GI tract and genitourinary
  - Lymphoreticular system

#### 438. What is your clinical diagnosis?

**Ans.** In view of the presentation of weakness of right half of the body with full recovery, the patient appears to be a case of young CVA (left) with right sided hemiplegia.

#### 439. What is the commonest cause of young CVA?

**Ans.** There is a long list of causes of young stroke but three common causes are;

1. CVA either due to embolism in a patient with RHD or some other form of heart disease or cerebral thrombosis or TIA or haemorrhage.
2. Head injury or trauma.
3. Procoagulant states;
  - Arteritis (SLE)
  - Antiphospholipid syndrome
  - Puerperium
  - Protein C or S deficiency
  - Hyperfibrinogenaemia

#### 440. What is hemiplegia? What are its various types?

**Ans.** Hemiplegia is defined as complete loss of motor functions (paralysis) on one half of the body; whereas partial loss of motor function is designated as *hemiparesis*. It is usually due to UMN lesion at any level from the cerebrum to spinal cord. The tracts involved are ascending and descending motor tracts especially the pyramidal tracts.

Hemiplegia is said to be complete if UMN 7th nerve palsy accompanies the hemiplegia and is considered incomplete in the absence of its involvement.

#### Terminology used for Hemiplegia

1. *Crossed hemiplegia*. It refers to ipsilateral LMN paralysis of one of the cranial nerves with contralateral (opposite side) hemiplegia. It signifies the brainstem as the site of the lesion.
2. *Uncrossed hemiplegia*. It refers to UMN 7th nerve palsy on the side of hemiplegia (i.e. both being opposite to cerebral lesion). For example, if UMN 7th nerve palsy and hemiplegia are on the left side, the cerebral lesion is on the right side.
3. *Dense hemiplegia*. The complete loss of voluntary functions (weakness) of equal magnitude in both upper and lower limbs on the side of the body involved constitutes dense hemiplegia. This signifies an internal capsular lesion as corticospinal fibres are condensed there.
4. *Pure motor hemiplegia*. Isolated unilateral involvement of corticospinal tract gives rise to pure motor hemiplegia. Usually, internal capsular lesion produces hemiplegia associated with hemianaesthesia. A

lacunar (small vessel) infarct of posterior limb of the internal capsule produces pure motor hemiplegia.

5. *Pseudobulbar palsy*. Bilateral corticospinal tracts involvement (double hemiplegia) in the medulla oblongata above the bulbar nuclei produces a syndrome of pseudobulbar palsy, which is characterised by dysarthria, dysphagia with bifacial paralysis and emotional lability. The jaw jerk is exaggerated.

Pure motor hemiplegia, pure sensory hemiplegia, ataxic hemiballismus syndrome and syndrome of pseudobulbar palsy are few examples of small vessel (lacunar) infarct.

6. *Stuttering hemiplegia*. Transient speech disturbance (aphasia, dysarthria) with hemiplegia indicates stuttering hemiplegia, is due to progressive occlusion of internal carotid artery (stroke-in-evolution). It ultimately results in completed stroke.
7. *Transient ischemic attack or transient hemiplegia*. It is sudden transient loss of motor function (paralysis) on one side of the body which recovers completely within 24 hours.
8. *Homolateral hemiplegia*. It means hemiplegia occurring on the same side of the lesion, is seen in unilateral cervical spinal cord lesion (Brown-Sequard's syndrome) because descending corticospinal tracts have already crossed at the level of the medulla, hence, they now represent the same side of cerebral hemisphere.

#### 441. What are the causes of hemiplegia?

**Ans.** The vascular diseases of the cerebrum (thrombosis, embolism, haemorrhage) exceed all other causes of hemiplegia. Trauma to the brain is second common cause followed by uncommon causes such as tumours, infections, demyelination and degenerative disorders (Table 1.114).

#### 442. What do you mean by the term stroke? How do you classify it?

**Ans.** A stroke is defined as a neurological deficit occurring as a result of CVA (atherosclerosis, thrombosis, embolism and haemorrhage). Stroke in clinical practice is used for haemiplegia but actually it implies more than that.

**Table 1.114:** Causes of hemiplegia**1. Organic causes****A. Cerebrovascular disease**

- Transient ischaemic attack (TIA)
- Progressive atherosclerosis (stroke-in-evolution, completed stroke)
- Internal carotid artery aneurysm or AV mal formations
- Cerebral thrombosis, embolism, haemorrhage
- Cerebral arteritis
- Dural sinus thrombosis

**B. Traumatic disorders**

- Brain contusion (concussion)
- Subdural haematoma

**C. Brain tumours****D. Infective disorders, e.g. brain abscess, meningitis, encephalitis, tuberculosis, syphilis****E. Demyelinating disorders**

- Multiple sclerosis

**2. Functional, e.g. hysteria****Classification**

1. **TIA.** It means transient hemiplegia or neurological deficit occurring as a result of ischaemia which recovers within 24 hours.
2. **Stroke-in-evolution.** The neurological deficit worsens gradually or in a step-wise pattern over hours or days
3. **Completed stroke.** Neurological deficit is complete at the onset and persists for days to weeks and often permanently.
4. **Reversible ischemic neurological deficit (RIND).** It means neurological deficit persisting for more than 24 hours but recovers totally within 3 weeks.
5. **Partial nonprogressive stroke.** As the name suggests, the neurological deficit is partial that persists for more than 3 weeks without any further progression.

**443. How will you localise the lesion in a case with hemiplegia?**

**Ans.** The site or the level of lesion can be deduced from associated neurological signs.

**1. Cortical or subcortical (corona radiata) lesion**

The cortical lesions usually produce monoplegia, hence, hemiplegia is of rare occurrence, but can occur if the cortical lesion extends downward into subcortical area (corona radiata). The characteristic features of cortical/subcortical lesion are:

- i. Contralateral hemiplegia of uncrossed type
  - ii. Convulsions (Jacksonian) may occur
  - iii. Speech disturbance (aphasia) if dominant hemisphere is involved. The dominant hemisphere is decided from handedness of a person. If a person is right-handed, the left hemisphere is dominant and contains the speech area.
  - iv. Cortical type of sensory loss (astereognosis, loss of sense of position, tactile localisation, and two-point discrimination)
  - v. Anosognosia, visual field defect
  - vi. Supranuclear 7th nerve palsy
2. **Internal capsular lesions**
    - Contralateral hemiplegia of uncrossed type
    - Contralateral hemianaesthesia
    - Dense hemiplegia – complete paralysis of face, upper and lower limbs
    - UMN paralysis of 7th nerve
    - No convulsion, no speech, taste or visual disturbance.

A pure motor isolated dense hemiplegia affecting simultaneously the face, arm and leg indicates a lesion in the posterior limb of internal capsule – a lacunar infarct

**3. Midbrain lesion**

- Contralateral hemiplegia of crossed type
- The 3rd nerve nuclear paralysis with contralateral hemiplegia constitutes *Weber's syndrome*
- Contralateral hemianaesthesia and analgesia

**4. Pontine lesion**

- Contralateral hemiplegia of crossed type
- Contralateral hemianaesthesia and analgesia
- Ipsilateral 6th or 7th cranial nerve paralysis (LMN type) with contralateral hemiplegia is called *Millard-Gubler syndrome*
- Constriction of pupil (*Horner's syndrome*) on the same side of the lesion due to involvement of sympathetic fibres
- Ataxic hemiplegia with or without dysarthria indicates a lacunar infarct

**5. Medulla oblongata lesion****A. Features of medial medullary syndrome****Ipsilateral**

- Paralysis of half of tongue (XII nerve palsy)

*Contralateral*

- Upper and lower limbs UMN paralysis sparing face
- Impaired tactile and proprioceptive sensations

**B. Features of lateral medullary syndrome (Wallenberg's syndrome)***Ipsilateral (same side of lesion)*

- Facial numbness (Vth nerve involvement)
- Ataxia, nystagmus (cerebellar involvement)
- Horner's syndrome (sympathetic involvement)
- IX and X nerve palsy
- Loss of posterior column sensations

*Contralateral (Opposite side)*

- Spinothalamic (pain, touch, temperature) sensory loss
- Hemiparesis (mild, unusual)

6. *Spinal cord (C<sub>1</sub>-C<sub>4</sub>) lesion*

- Brown-Sequard syndrome (Read spinal cord lesion).

**444. How will you evaluate an unconscious patient for evidence of hemiplegia?**

**Ans.** The evaluation includes:

**Head and Neck**

Patient should be examined for evidence of trauma and neck stiffness.

**Pupils**

1. *Fixed dilatation of one pupil* indicates herniation of uncus of temporal lobe (coning) and compression of third nerve. This could be due to raised intracranial tension or may be observed during lumbar puncture in a patient with raised intracranial tension if precautions are not exercised for slow decompression.
2. *'Pinpoint' pupils.* 'Fixed pin-point pupils' occur in pontine lesion (pontine haemorrhage) due to sympathetic involvement
3. *Mid-dilated pupils.* Fixed mid-dilated pupil may be seen in midbrain lesion
4. *Horner's syndrome* (Ipsilateral pupillary constriction, ptosis, enophthalmos, anhidrosis, loss of ciliospinal reflex) occurs with lesions of the hypothalamus and also in "coning".

**Ocular Fundi**

These should be examined for papilloedema

**Vestibulo-ocular Reflex (Doll's Head Reflex)**

Passive head rotation causes conjugate deviation of eyes in the direction opposite to the induced head movement (doll's head reflex). This reflex is lost in deep coma. It is absent in brainstem lesions.

**Abnormalities of Conjugate Deviation**

- i. Sustained conjugate lateral gaze occurs towards the side of a destructive hemispheric lesion (i.e. the eyes look towards normal limbs)
- ii. In pontine lesion, sustained conjugate lateral gaze occurs away from the side of lesion, i.e. 'towards the paralysed limbs'
- iii. Skew deviation (one eye rolled upwards and the other downwards) is a rare sign, indicates brainstem lesions
- iv. Ocular bobbing. These are sudden, brisk, downward—diving eye movements seen in pontine or cerebellar haemorrhage.

**Motor System Examination**

- In hemiparesis, there is abnormal flaccidity of the limbs on the affected side. Raise both the upper limbs and then release them suddenly, the paralysed limb falls to the ground with a thud rapidly than non-paralysed limb
- Facial asymmetry (drooping of one side of face), unilateral dribbling, or blowing in and out of the paralysed cheek indicate 7th nerve palsy
- Asymmetry of tendon reflexes. In deep coma, the reflexes may be absent and even plantars are extensor. Occasionally, asymmetry of reflexes helps to point out the side of lesion
- Decerebrate or decorticate posture indicates cerebral lesion.

**445. What is hysterical hemiplegia?**

**Ans.** In hysterical hemiplegia, the patient drags the affected leg along the ground behind the body and does not circumduct the leg or use it to support the body weight. At times, hemiplegic leg is pushed ahead of the patient and used mainly for support. The arm on the affected side remains limp and is kept by the side of the body and does not develop flexed posture commonly



seen in hemiplegia from organic causes (Fig. 1.33). The characteristic signs of hysterical hemiplegia are:

1. *Hysterical gait*
2. *Normal tone*. The affected limbs show normal resistance to passive manipulation or there may be increasing resistance being offered by the patient as limb is being moved. The patient is asked to move the limb, the movement is seen to be slow and jerky, often with contraction of both agonist and antagonist muscles simultaneously or intermittently.
3. The *tendon reflexes* are normal on both the sides
4. *Plantars* are flexor or down-going
5. Often there is *loss of all forms of sensations* (touch, pain, smell, vision and hearing) on the paralysed side—a group of sensory changes that is never seen in organic brain disease.
6. *Hoover's sign and Babinski's combined leg flexion tests* are helpful in distinguishing hysterical from organic hemiplegia.

“To elicit *Hoover's sign*, the supine patient is asked to raise one leg from the bed against resistance. In a normal individual the back of heel of contralateral leg presses firmly down, and the same is true for organic hemiplegia when attempts are made to lift the paralysed leg. The hysterical patient will press down the supposedly paralysed limb more strongly under these circumstances which can be appreciated by placing a hand below the normal heel.

In *Babinski's combined leg flexion test*, the patient with organic hemiplegia is asked to sit up on the bed from lying down position without using his/her arms; in doing this, the paralysed leg flexes (if power is good) at the hip and heel is lifted from the bed, while the heel of the normal leg is pressed into the bed which is appreciated by putting the hand below the heel. This sign is absent in hysterical hemiplegia”.

**446. How will you proceed to diagnose a case of hemiplegia? What clinical conditions will you keep in mind in a case with hemiplegia?**

Ans. Clinical evaluation of hemiplegia rests on history, clinical examination and investigations. A protocol of questionnaire is given in Table 1.115. The differential diagnosis includes to find out its cause and to localise the site of the lesion. Functional disorders such as

**Table 1.115:** Clinical evaluation of a case with hemiplegia

Note the followings;

- Age
- Onset- acute (sudden, catastrophic) subacute or chronic  
Acute onset suggests cerebral haemorrhage
- *Disturbance in consciousness*. Majority of the patients with cerebral thrombosis and embolism retain consciousness
- Disturbance of speech (aphasia, dysarthria, dysphonia)
- History of nasal regurgitation, drooling of saliva from the angle of the mouth, facial asymmetry
- Trauma
- Convulsions- Generalised convulsions preceding the paralysis; Todd's paralysis (postictal) indicate ICSOL (intracranial space occupying lesion), hypertensive encephalopathy. Convulsions, fever and paralysis indicate meningitis, cerebral abscess, encephalitis
- Disturbance of smell, taste, vision (visual field defect, diplopia)
- Headache – severe, persistent or mild. Severe headache associated with hemiplegia points out either subarachnoid haemorrhage or cerebral haemorrhage or hypertensive encephalopathy. Headache preceding paralysis suggests ICSOL or subdural haematoma
- History of diabetes, hypertension, familial hyperlipidemia, obesity, pregnancy, delivery (puerperium), bleeding or coagulation disorders, hypercoagulable states, etc.
- Symptoms and signs of cardiovascular and pulmonary disease
- Symptoms and signs of infections
- Symptoms and signs of raised intracranial tension

hysterical hemiplegia should be differentiated from organic one.

**447. How will you describe the complete diagnosis in a case with hemiplegia?**

Ans. The complete diagnosis includes:

- Clinical diagnosis such as CVA left side with hemiplegia right side
- Site of lesion—internal capsule
- Net neurological deficit, e.g.
  - Pyramidal tract
  - Posterior column
  - Spinothalamic tract
  - Type of lesion, e.g. vascular (middle cerebral artery thrombosis, embolism, etc.)
- Aetiology—atherosclerotic or embolic from heart lesion.

The common clinical conditions that come to the mind are vascular lesions, i.e. (i) cerebral thrombosis, (ii) cerebral haemorrhage, (iii) cerebral embolism; space



**Table 1.116:** Differential diagnosis of cerebrovascular accidents with hemiplegia

Features	Cerebral thrombosis	Cerebral embolism	Cerebral haemorrhage
Onset	Sudden, may be slow (stroke-in-evolution)	Abrupt like bolt from the blue	Sudden, catastrophic
Premonitory symptoms	May be present in the form of TIA	Absent	May be present in the form of speech disturbance or attacks of weakness in a limb
Consciousness	Preserved or there may be slight confusion	Preserved, sometimes patient may be dazed or drowsy	Usually semiconscious or unconscious
Headache	Absent but occurs if cerebral oedema develops	Absent	Severe, persistent
Neck stiffness	Absent	Absent	Present if bleed leaks into subarachnoid space
Neurological deficit	Slowly developing	Maximum at the onset, followed by initiation of recovery	Rapidly developing and progressive
Precipitating or predisposing conditions	Hypertension, diabetes, dyslipidaemia, hypothyroidism, hypercoagulable states (pregnancy, puerperium, oral contraceptives), dehydration or shock	Evidence of source of embolisation, i.e. heart disease (ischaemic, rheumatic), aneurysm (arterial, ventricular), thrombosis (atherosclerosis, atrial)	Precipitated by stress, exertion, physical act, sudden rise in BP. Atheromatous arteries, aneurysm of arteries or AV malformations predispose to haemorrhage
Symptoms and signs of raised intracranial tension	Absent	Absent	May be present if bleed leaks into subarachnoid space
Recovery	Slow, may be partial or complete	Rapid, recovery is the rule	Slow, if patient recovers. Residual damage persists

occupying lesion, demyelinating and degenerative lesion and functional disorders. The three common cerebrovascular lesions that can produce hemiplegia are compared in Table 1.116.

**448. What are the characteristic features of hemiplegia due to a brain tumour? What are false localising signs?**

**Ans.** They are given in Table 1.117.

**449. What are features of hemiplegia due to chronic subdural haematoma?**

**Ans.** The features of hemiplegia in chronic subdural haematoma are:

- There may be history of injury or fall. Patient may have underlying liver disease, bleeding diathesis or may be on anticoagulants
- Slow or chronic onset with fluctuating headache, slow thinking, confusion, drowsiness, personality changes, seizures, etc

**Table 1.117:** Hemiplegia due to brain tumour

- Slow onset and slow progression
- Focal symptoms – Jacksonian fits (focal epilepsy), aphasia, hemiplegia or monoplegia
- Symptoms and signs of raised intracranial tension, e.g.
  - Headache, vomiting, papilloedema
  - Bradycardia, slight rise in BP, rise in respiratory rate
  - Mental features – confusion, disorientation, emotional apathy, depression, somnolence, urinary and faecal incontinence
  - Epileptic seizures
  - False localising sign
    - Unilateral 6th nerve palsy (diplopia with lateral deviation of the eye), sometimes it may be bilateral
    - Bilateral plantar extensor response
    - Bilateral grasp reflexes
    - Cerebellar signs
    - Fixed dilated pupils
- There may be lucid interval (weeks, months or more than a year) between the onset of injury and symptoms

- iv. Hemiplegia is uncrossed, due to compression effect on pyramidal tracts
- v. Symptoms and signs of raised intracranial tension
- vi. Hemianopia, hemianaesthesia, aphasia, epilepsy are seldom observed as structures subserving these functions are deeply situated and are not compressed easily.

**450. List the predisposing factors for CVA (hemiplegia).**

**Ans.** The following are the risk factors for accelerated atherogenesis predisposing to cerebral thrombosis (CVA). These must be taken into account in the past/ present history (Table 1.118).

**Table 1.118:** Risk factors in CVA

- Systemic hypertension
- Diabetes
- Hyperlipidaemia (familial or nonfamilial)
- Homocysteinaemia and homocysteinuria
- Deficiency of proteins C and S
- Strong family history
- Smoking
- Obesity
- Oral contraceptives
- Hyperviscosity syndrome, e.g. polycythemia, antiphospholipid syndrome
- Increasing age (old age)

**451. What are features of atherosclerosis?**

**Ans.** Following are the features:

- Age >60 years
- There may be past history of IHD/TIA/intermittent claudication
- Risk factor may be present (Table 1.118 above)
- The radial pulse or other vessel walls may be thickened and palpable
- There may be suprasternal pulsations
- Weak carotids and even a bruit may be present
- Signs of hyperlipidaemia (e.g. xanthomas or xanthelasma) may be evident occasionally
- Signs of senility, e.g. wrinkled face, corneal arcus, frontal baldness may be present
- Fundus examination may reveal arteriosclerotic changes (A:V nipping)
- BP may show systolic hypertension
- Chest X-ray may reveal unfolding or calcification of arch of aorta (ring shaped calcification).

**452. What are causes of recurrent CVA/ hemiplegia?**

**Ans.** Causes are:

- TIA (transient ischaemia attack) is common cause
- Post-epilepsy – Todd's paralysis
- Hypertensive encephalopathy
- Migrainous hemiplegia (vasospastic hemiplegia)
- Hysterical hemiplegia.

**453. What are the causes of stroke in young?**

**Ans.** Causes are:

- Cerebral embolism from a cardiac source, commonly rheumatic valvular disease
- Subarachnoid haemorrhage (rupture of Berry aneurysm or AV malformations or anticoagulant therapy)
- Hyperviscosity syndrome, e.g. polycythaemia, post-partum state, oral contraceptive
- Arteritis, e.g. tubercular, syphilitic, Takayasu's disease, collagen vascular disease
- Premature or accelerated atherogenesis, e.g. familial hyperlipidaemia, hypertriglyceridaemia, diabetes, nephrotic syndrome, hypothyroidism
- Demyelinating disease, e.g. multiple sclerosis
- Head injury
- Inflammatory disease, e.g. meningitis, encephalitis, cerebral abscess, tuberculoma, cerebral malaria
- Migrainous
- Intracranial neoplasm, e.g. primary or secondary
- Procoagulant states, e.g. protein C and S deficiency, homocysteinaemia, antithrombin –1 deficiency, antiphospholipid syndrome.

**454. What are bladder and bowel disturbances in the hemiplegia?**

**Ans.** Unilateral involvement of bladder usually does not produce much symptoms, hence, in hemiplegia, there can be either hesitancy or precipitancy. In unconscious patient with hemiplegia, condom drainage or indwelling catheterisation is necessary to prevent bed-wetting

**455. What is the usual clinical course of hemiplegia?**

**Ans.** A patient of hemiplegia may pass through the following stages:

1. *Stage of neuronal shock.* It is state when the reflex activity is suppressed, i.e. there is hypotonia. Jerks

**Table 1.119:** Blood supply of internal capsule

<i>Limb</i>	<i>Upper half</i>	<i>Lower half</i>
Anterior	Middle cerebral artery	Anterior cerebral artery
Posterior	Middle cerebral artery	Anterior choroidal and Posterior communicating artery

are absent and plantars are silent. This stage may not be seen in all cases of hemiplegia, but commonly seen in acute onset hemiplegia. This lasts for 2-3 weeks

2. *Stage of recovery:* After 2-3 weeks, the recovery starts. The face recovers first. Power returns in the extensors of lower limb and flexors of the upper limb. Finer movements of the fingers and hand recover last to a variable extent.
3. *Stage of residual paralysis.* The only deficit is little spasticity and a hemiplegic gait.

#### 456. What is blood supply of internal capsule?

**Ans.** Blood supply of internal capsule are described in Table 1.119.

#### 457. What is anterior cerebral artery syndrome?

**Ans.** Occlusion of anterior cerebral artery (anterior cerebral artery syndrome) produces certain clinical features depending on the site of block such as:

<i>Symptoms and signs</i>	<i>Area involved</i>
Monoplegia involving lower limb and paresis of opposite arm to lesser degree (incomplete hemiplegia)	Motor leg area. Arm area of cortex or its descending fibres in corona radiata
Loss of cortical sensations over lower limb involved	Sensory leg area
Urinary in continence	Paracentral lobule (bladder area)
Contralateral primitive reflexes, e.g. grasp, sucking present	Supplemental motor area
Akinetic mutism	Cingulate gyrus
Gait apraxia	Frontal cortex near leg area

#### 458. How will you investigate a patient with hemiplegia?

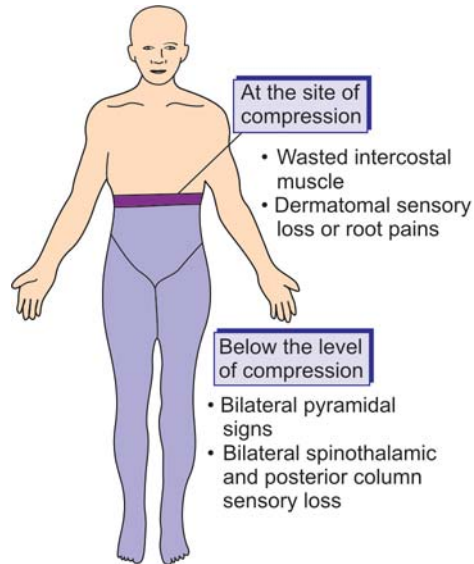
**Ans.** Investigations are done for diagnosis, to find out the underlying cause and risk factors. They are given in Table 1.120.

**Table 1.120:** Investigations for a patient with hemiplegia

<i>Purpose</i>	<i>Test(s)</i>
1. For vascular episode	CT scan/MRI
2. For underlying vascular cause	ECG, cardiac ultrasound, MRA, (MR angiography) Doppler ultrasound, carotid angiography
3. For risk factors	Blood count, serum cholesterol, blood glucose, clotting or thrombophilia screen

### CASE 34: PARAPLEGIA

A patient (not shown) presented with weakness of both lower limbs which was slowly progressive with difficulty in passing urine. There was history of numbness of both the lower limbs below the umbilicus. There was no history of fever or trauma preceding to this illness. The physical signs of the patients are diagrammatically represented in Fig. 1.34.



**Fig. 1.34:** Compression paraplegia with transverse thoracic spinal cord lesion with definite level. There are UMN signs below the site of compression. There is bilateral loss of all sensory modalities below the level of compression

#### History—Points to be Noted

- Note date and time of onset of paralysis
- Mode of onset (sudden or gradual)
- Precipitating factors, e.g. spinal trauma, vaccination
- Progress of paralysis, e.g. increasing, stationary, progressive, waxing or waning type
- Motor symptoms including inability or difficulty in walking
- Sensory symptoms, e.g. root pain, sensation of pins and needles, numbness, history of a constriction band around the waist.

#### Past history

Ask for;

- History of fever, tuberculosis, exposure to STD
- History of similar episodes in the past
- History of spinal trauma
- History of diabetes, HT
- History of alcoholism
- Pain in back

Family history

- Diabetes, HT
- History of paraplegia in other members of the family
- Tuberculosis

#### Clinical Presentations

- Weakness of both lower limbs
- Numbness of both lower limbs
- Difficulty in passing urine and stool

#### Unilateral Compression

(Brown-Sequard syndrome) The signs are:

- Ipsilateral in the side compression) pyramidal signs
- Contralateral (opposite to the side involved) spinothalamic sensory loss of pain, touch and temperature

#### Examination

##### 1. General physical: Note the following;

- Consciousness or cooperative, posture
- Neck for lymphadenopathy
- Vitals, e.g. pulse, BP and temperature
- Skin, e.g. pigmentation, neuro-fibroma

##### II. Nervous system. Examine;

- Higher functions
- Neck rigidity
- Cranial nerves
- Cerebellar functions
- Motor system including gait
- Sensory system

##### III. Examination of spine

- Kyphosis, scoliosis, gibbus, tenderness and spina bifida (a tuft of hair)

##### IV. Other systems

- Respiratory system examination for tuberculosis, bronchogenic carcinoma and lymphoma
- CVS-as discussed in hemiplegia
- GI tract for hepatosplenomegaly, ascites
- Lymphoreticular system for sternal tenderness, haemorrhagic spots and lymphadenopathy

#### 459. What is your clinical diagnosis?

**Ans.** Presence of UMN signs in both lower limbs with localised LMN signs over the lower part of chest, suggest the provisional diagnosis of compression paraplegia.

#### 460. What does paraplegia mean?

**Ans.** It refers to complete loss of motor functions (paralysis) of both lower limbs. Partial weakness is designated as *paraparesis*.

**Table 1.121:** Distinction between paraplegia-in-extension and paraplegia-in-flexion

Feature	Paraplegia-in-extension	Paraplegia-in-flexion
Posture	Lower limbs adopt an extension posture and extensor muscles are spastic. Extensor spasms occur	Lower limbs adopt flexed posture. Intermittent flexor spasms occur in which there is flexion of both lower limbs
Neurological deficit	Only pyramidal tracts involved	Both pyramidal and extrapyramidal tracts are involved
<i>Clinical features</i>		
Positions of limbs	Hip extended and adducted, knee extended and feet plantar-flexed	Thigh and knee flexed, feet dorsiflexed
Tone	Clasp-knife spasticity in extensor groups of muscles	Rigidity in flexor groups of muscles
Tendon jerks	Exaggerated	Diminished
Plantar response	Extensor	Extensor but evokes flexor spasms
Incontinence of bowel and bladder	Absent	Present
Mass reflex*	Absent	Present

**N.B.** \*Mass reflex is an enlarged area of hyperexcitability of reflex activity. Just stroking the skin of either lower limbs or lower abdominal wall, produces the reflex evacuation of the bladder and bowel with reflex flexor spasms of the lower limbs and lower trunk muscles.

#### 461. What is cerebral paraplegia? What are its causes?

**Ans.** The lower limbs and bladder (micturition centre) are represented in paracentral lobule (about upper one inch of cerebral cortex), hence, lesion of this area produces paraplegia with bladder disturbance (retention urine) and cortical type of sensory loss. There may be associated headache, vomiting and convulsions or Jacksonian fits.

The **causes** are:

- Cerebral diplegia
- Superior sagittal sinus thrombosis
- Parasagittal meningioma
- Thrombosis of unpaired anterior cerebral artery
- Gun shot injury of paracentral lobule
- Internal hydrocephalus

#### 462. What is spastic paraplegia?

**Ans.** The involvement of spinal cord and cerebrum produces spastic (UMN) paraplegia. Spastic paraplegia is of two types;

- *Paraplegia-in-extension*
- *Paraplegia-in-flexion*

The difference between paraplegia-in-extension and paraplegia-in-flexion are summarised in Table 1.121.

#### 463. What is clinical course of compression paraplegia?

**Ans.** Initially, due to involvement (compression) of pyramidal tracts, there is *paraplegia-in-extension* due to increased tone of antegravity muscles as a result of intact extrapyramidal system. When extrapyramidal system is involved (tectospinal, rubrospinal, vestibulospinal), the paraplegia-in-flexion develops resulting in flexors spasms, contractures and deformity (Table 1.121).

#### 464. What is flaccid paraplegia?

**Ans.** Flaccid papralysis means lower motor neuron type of paralysis resulting from the diseases involving anterior horns cells, radicals, peripheral nerves and muscles (Table 1.122). Acute onset of UMN type of paralysis may be

**Table 1.122:** Causes of flaccid paralysis

Sites	Causes
<ul style="list-style-type: none"> <li>• Anterior horn cells</li> <li>• Nerve root</li> </ul>	Poliomyelitis Radiculitis, polyradiculoneuropathy, tabes dorsalis, Cauda equina
<ul style="list-style-type: none"> <li>• Peripheral nerves</li> </ul>	GB syndrome, peripheral neuropathies
<ul style="list-style-type: none"> <li>• Myoneural junction</li> </ul>	Myasthenic gravis, Myasthenia-myopathic syndrome (Lambert-Eaton syndrome) periodic paralysis (hypo or hyperkalaemic)
<ul style="list-style-type: none"> <li>• Muscles</li> </ul>	Myopathy



flaccid instead of spastic if patient is in shock state. A hysterical patient may also present with LMN type of paraplegia. The cause are summarised in Table 1.122.

**465. What are the causes of spastic paraplegia?**

**Ans.** It may be due to compression of the spinal cord or without it. Spinal cord tumours are the most common cause of compression (Table 1.123).

The central causes of spastic paraplegia have already been listed.

**466. How will differentiate between extramedullary and intramedullary spinal cord compression?**

**Ans.** Table 1.124 differentiates between these two spinal cord compressions.

**467. How will you calculate the level of spinal segments in relation to vertebra in a case with compression paraplegia?**

**Ans.** In case of compression, if vertebra involved is known, then calculation of spinal segment is done as follows:

Vertebra	Spinal segment
For cervical vertebrae	: Add 1
For 1-6 thoracic vertebrae	: Add 2
For 7-9 thoracic vertebrae	: Add 3
The T <sub>10</sub> vertebra overlies	: L <sub>1</sub> and L <sub>2</sub>
The T <sub>11</sub> vertebra overlies	: L <sub>3</sub> and L <sub>4</sub>
The T <sub>12</sub> vertebra overlies	: L <sub>5</sub> segment

**Table 1.123:** Common cause of spastic paraplegia

<b>I. Compressive</b>
<b>A. Extramedullary</b>
<b>i. Intradural</b>
• Meningioma, neurofibroma, arachnoiditis
<b>ii. Extradural</b>
• Pott's disease (caries spine)
• Vertebral neoplasms, e.g. metastases, myeloma
• Pachymeningitis
• Prolapsed intervertebral disc
• Epidural abscess or haemorrhage
• Fracture dislocation of vertebra, Paget's disease, osteoporosis
<b>B. Intramedullary</b>
• Syringomyelia, haematomyelia
• Intramedullary tumour, e.g. ependymoma, glioma
• Spinal cord abscess (e.g. pyogenic, tuberculosis)
<b>II. Non-compressive</b>
• Motor neurone disease especially amyotrophic lateral sclerosis
• Multiple sclerosis, postvaccinal myelitis
• Acute transverse myelitis
• Subacute combined degeneration (Vit. B <sub>12</sub> deficiency)
• Lathyrism
• Syringomyelia
• Hereditary spastic paraplegia
• Tropical spastic paraplegia
• Radiation myelopathy

- The L1 overlies the sacral and coccygeal segments.

**NB:** If spinal segment involved is known than vertebral level can be calculated as detailed above.

**Table 1.124:** Differentiation between extramedullary and intramedullary spinal cord compression

Feature	Extramedullary	Intramedullary
Root pain	Common	Rare
UMN signs	Early and prominent	Late feature and are less prominent
LMN signs	Segmental at the site of compression	Extends to involve few segments with atrophy and fasciculations
Reflexes	Brisk, early feature	Less brisk, late feature
Sensory deficit	Contralateral loss of pain and temperature with ipsilateral loss of proprioception	Dissociated sensory loss
Sacral sparing	Absent	Present
Bowel and bladder involvement	Late	Early
Trophic changes	Unusual	Common
Vertebral tenderness	May be present	Absent
CSF changes	Forin's syndrome common	Rare

**468. What is hemisection of spinal cord?**

**Ans.** The characteristic features of the hemisection of spinal cord are:

*Brown-sequard syndrome* It is hemi-section of spinal cord, commonly due to gun shot injury. It consists of;

- Contralateral loss of pain and temperature with ipsilateral loss of posterior column sensations
- Monoplegia or hemiplegia on the same side of the lesion below the site of involvement
- UMN signs below the level of lesion i.e. exaggerated tendon jerks and plantar extensors. Superficial reflexes are lost
- A band of hyperaesthesia at the level of compression.

**469. How will you distinguish compressive from noncompressive myelopathy?**

**Ans.** The absolute characteristic of compression of the cord is either motor loss (loss of tendon jerk, muscle wasting, fasciculations) or a sensory sign (hyperesthesia, analgesia) at the site of compression while no such phenomenon is seen in noncompressive myelopathy. The distinction between the two is tabulated (Table 1.125).

**Table 1.125:** Distinction between compressive and noncompressive myelopathy

Compressive	Non-compressive
Bone changes, i.e. deformity, tenderness present	No bony change
Girdle like pain present (root pain)	No root pain
Upper level of sensory loss present	No definite level
Zone of hyperaesthesia may be present	Absent
Usually of gradual onset	Usually of acute onset
Asymmetrical involvement of limbs	Symmetrical involvement of limbs
Flexor spasms common	Absent
Bowel and bladder involvement is early	Late involvement
Commonest cause is caries spine	Commonest cause motor neuron disease

### Read Neurological Examination in Clinical Method in Medicine by Dr SN Chug

- Grading of power
- UMN signs
- LMN signs

**470. What are the causes of cord compression at multiple sites?**

**Ans.** Following are the causes:

- Arachnoiditis (tubercular—there is patchy involvement)
- Neurofibromatosis
- Multiple discs prolapse
- Secondary deposits
- Cervical spondylosis

**471. What are the causes of paraplegia without sensory loss?**

**Ans.** Causes are:

- Hereditary spastic paraplegia
- Lathyrism
- GB syndrome
- Amyotrophic lateral sclerosis
- Fluorosis

**472. What are the causes of paraplegia with loss of deep tendon jerks?**

**Ans.** In paraplegia, the tendon jerks are brisk. They can only become absent when either patient is in spinal shock or there is involvement of afferent or efferent side of the reflex arc. The causes are:

- Neuronal shock (spinal shock). All jerks are absent
- Radiculitis—the jerk whose root is involved will be absent
- Peripheral neuropathy—bilateral ankle jerk will be absent
- Presence of bed-sores or complicating UTI. The reflex activity in this complication may be suppressed leading to loss of most reflexes
- Hematomyelia (sudden haemorrhage from AV malformation) or myelomalacia cause loss of reflexes.

**473. What are the causes of Quadriplegia?**

**Ans.** Quadriplegia means weakness of all the four limbs. Therefore, cause may lie in the brain or spinal cord anywhere from the cortex to spinal level T<sub>1</sub>. The lesion must be bilateral. The causes are;

1. Cerebral palsy
2. Bilateral brainstem lesion
3. High cervical cord compression, e.g. craniocervical anomaly, high spinal cord injury, etc.
4. Multiple sclerosis

5. Motor neuron disease
6. Acute anterior poliomyelitis
7. Guillain-Barré syndrome
8. Peripheral neuropathy
9. Myopathy or polymyositis
10. Periodic paralysis (transient quadriplegia).

**474. What are the causes and clinical features of high cervical cord compression?**

**Ans.** The features of high cervical cord compression are tabulated in Table 1.126.

**Table 1.126:** Features and causes of high cervical cord compression

<b>Causes</b>
1. <i>Craniovertebral anomalies</i> , e.g. platybasia, basilar impression, atlantoaxial dislocation, Klippel-Feil anomaly, Arnold-Chiari malformation
2. <i>High cervical cord (C1-C4) lesion</i> , e.g. due to craniovertebral anomaly, fracture dislocation, haematomyelia, cervical spondylosis, cord tumours, caries spine.
<b>Features</b>
<ul style="list-style-type: none"> <li>• A triad of short neck, low hair line and restricted cervical movements</li> <li>• Spastic quadriparesis of gradual onset, involving one limb followed by the other or</li> <li>• Spastic paraplegia with;               <ul style="list-style-type: none"> <li>Horner's syndrome</li> <li>XI nerve palsy</li> <li>V nerve palsy (spinal tract of Vth) nerve leading to loss of sensation over face e.g. 1st and 2nd division of V)</li> <li>Vertical nystagmas</li> </ul> </li> <li>• Cerebellar signs may be present</li> <li>• Mirror image movement, impaired sense of position and vibration</li> </ul>

**475. How will you localise of the lesion in compressive myelopathy?**

**Ans.** Diagnostic clues to lesions at different sites are depicted in Table 1.127.

**476. How do you differentiate between conus medullaris and cauda equina syndrome?**

**Ans.** The conus medullaris is the terminal portion/ point at which spinal cord ends and cauda equina (a bunch of roots) starts. Therefore, the main distinctions between the two is the plantars extensor and symmetrical LMN signs in conus medullaris; while plantar are flexor or not elicitable with asymmetric LMN paralysis in cauda equina syndrome (Table 1.128).

**Table 1.127:** Lesions at different sites and their signs

Site of lesion (spinal segment)	Symptoms and signs
<i>High cervical cord lesion e.g. at C<sub>1</sub>-C<sub>4</sub></i>	<ul style="list-style-type: none"> <li>• UMN quadriplegia</li> <li>• There may be weakness of respiratory muscles or diaphragmatic palsy</li> <li>• There may be suboccipital pain radiating to neck and shoulder</li> </ul>
<i>Lesion at C<sub>4</sub>-C<sub>5</sub></i>	Quadriparesis without respiratory or diaphragmatic palsy
<i>Lesion at C<sub>5</sub>-C<sub>6</sub></i>	<ul style="list-style-type: none"> <li>• Quadriplegia (UMN type)</li> <li>• Loss of biceps and supinator reflexes</li> <li>• Inversion of supinator indicates lesion at C<sub>5</sub></li> </ul>
<i>Lesion at C<sub>7</sub>-C<sub>8</sub></i>	<ul style="list-style-type: none"> <li>• UMN quadriparesis</li> <li>• Normal biceps and supinator jerks</li> <li>• Loss of triceps and finger flexion reflexes</li> <li>• There is paralysis of finger and wrist flexion</li> </ul>
Note: Horner's syndrome may occur at any level of cervical cord compression	
<i>Lesion above T<sub>6</sub></i>	<ul style="list-style-type: none"> <li>• Paraplegia with loss of all abdominal reflexes</li> <li>• There is a level of sensory loss over the chest</li> <li>• Deep tendon reflexes below compression are exaggerated and plantars are extensor</li> </ul>
<i>Lesion T<sub>7</sub>-T<sub>9</sub></i>	• Paraplegia (UMN) with loss of upper abdominal reflexes
<i>Lesions at T<sub>9</sub>-T<sub>10</sub></i>	• Umbilicus is turned downwards during rising test (Beever's sign)
<i>Lesion T<sub>10</sub>-T<sub>12</sub></i>	<ul style="list-style-type: none"> <li>• Paralysis of both lower limbs (UMN type of paraplegia)</li> <li>• Upper abdominal reflexes are spared but lower abdominal reflexes are lost</li> <li>• Umbilicus is turned upwards during rising test due to paralysis of lower part of rectus abdominis. (Beever's sign actually indicates lesions at T<sub>9</sub> and T<sub>10</sub>)</li> </ul>
<i>Lesion of L<sub>1</sub> and L<sub>2</sub></i>	<ul style="list-style-type: none"> <li>• Paraplegia (UMN) with loss of cremasteric reflex</li> <li>• Deep tendon jerks below the level of compression exaggerated</li> </ul>
<i>Lesion of L<sub>3</sub>-L<sub>4</sub></i>	• Paraplegia with loss of knee jerks and preservation of ankle jerks
<i>Lesion of L<sub>5</sub> and S<sub>1</sub></i>	• Paralysis of movements of foot and ankle, flexion at knee and extension of thigh. There is loss of ankle jerks

**Table 1.128:** Differentiating features between conus medullaris and cauda equina syndrome

<i>Conus medullaris lesion</i>	<i>Cauda equina syndrome</i>
Bilateral symmetrical involvement of both lower limbs	Asymmetric involvement of both lower limbs
No root pain	Severe low back or root pain
No limb weakness	Asymmetric limb weakness
Bilateral saddle anaesthesia	Asymmetric sensory loss
The bulbocavernosus (S <sub>2</sub> -S <sub>4</sub> ) and anal reflexes (S <sub>4</sub> -S <sub>5</sub> ) are absent	Variable areflexia depending on the roots involved
Bladder and bowel disturbance common	They are relatively spared
Plantars are extensor but not always	Plantars are normal or not elicitable

**477. What are symptoms and signs of spinal cord compression?**

**Ans.** In spinal cord compression, certain symptoms and signs (motor and sensory) appear at the site of compression as well as below the compression (Table 1.129).

**478. What are classical features of acute transverse myelitis?**

**Ans.** Following are classical features:

- Acute onset of fever with flaccid paralysis. There may be neck or back pain
- Cause is mostly viral
- Bladder involvement is early
- Girdle constriction (constriction band) around the waist is common indicating mid-thoracic region as the common site of involvement
- Variable degree of sensory loss (complete or incomplete) below the level of the lesion. A zone of hyperesthesia may be present between the area of sensory loss and area of normal sensation
- There is loss of all tendon reflexes (areflexia) due to spinal shock. Abdominal reflexes are absent. Plantar are not extensors. As the spinal shock passes off, hyper-reflexia returns with plantar extensor response.

**479. What are causes of episodic weakness?**

**Ans.** Causes are:

- Myasthenia gravis
- Hyperthyroidism
- Periodic paralysis (hypokalaemic, hyperkalaemic)

**Table 1.129:** Symptoms and signs of spinal cord compression**Symptoms**

1. **Pain:** Localised pain over the spine or in a root distribution which may be aggravated by coughing, sneezing or straining. Girdle-like sensation or sense of constriction band at the level of lesion suggests posterior column involvement
2. **Sensory:** Paraesthesia or numbness in the lower limbs which spreads upwards
3. **Motor:** Weakness, heaviness or stiffness of the limbs most commonly the legs
4. **Sphincters:** Urgency or hesitancy of micturition leading eventually to urinary retention

**Signs****1. Sensory deficit**

- A. *At the level of compression:* A zone of hyperesthesia or hyperalgesia points towards the level of compression
- B. *Below the level of compression:* There is loss of sensations carried by spinothalamic tracts and posterior columns

**2. Motor**

- A. *At the level of compression*
  - Atrophy of a muscle
  - Loss of a deep tendon reflex, if the segmental supply of the reflex is interrupted
  - The loss of lower abdominal reflex with preservation of upper abdominal reflex indicates the lesion at T<sub>9</sub>-T<sub>10</sub>
- B. *Below the level of lesion*
  - All deep tendon reflexes exaggerated
  - All superficial reflexes lost
  - Tone increased, power decreased
  - Plantars are extensor
  - Retention of urine

- Conn's syndrome (primary hyperaldosteronism)
- Botulinum poisoning
- Guillain-Barré syndrome

**480. What is Lathyrism?**

**Ans.** It is a slowly evolving epidemic spastic paraplegia due to consumption of 'khesari dal' (lathyrus sativus) for prolonged period. It occurs in areas where drought are commonly seen, e.g. UP, Bihar, Rajasthan and MP where poor people consume often a mixture of wheat, Bengal gram and Khesari dal – called "birri". It may involve many families in a locality. The causative factor is BOAA – a neurotoxin. Initially, patients complain of nocturnal muscle cramps, stiffness of limbs and inability to walk. Ultimately due to increasing spasticity they pass through one-stick stage (scissor type gait), two-stick stage (patient uses two sticks to walk) and crawler stage (patient crawls on hands).

**481. What are causes of optic atrophy and paraplegia?**

**Ans.** Optic atrophy may be part and parcel of the disease causing paraplegia.

- Hereditary (Friedreich's ) ataxia
- Neuromyelitis optica (Devic's disease—a demyelinating disorder)
- Eale's disease
- Subacute myelo-optic neuropathy, alcohol-induced
- Infections-like tuberculosis and syphilis
- Deficiency states, e.g. subacute combined degeneration, pellagra.

**482. How does tuberculosis cause paraplegia?**

**Ans.** This is as follows:

1. Compression of the cord by cold abscess (extradural compression)
2. Tubercular arachnoiditis or pachymeningitis
3. Tubercular endarteritis (vascular phenomenon) producing myelomalacia of the cord
4. Tubercular myelitis, i.e. extension of the lesion from outside to within.

**483. How will you investigate the case with paraplegia?**

**Ans.** Investigations are:

1. *Routine blood tests* (TLC, DLC, ESR)
2. *Urine examination*, urine for culture and sensitivity
3. *Blood biochemistry*, e.g. urea, creatinine, electrolytes
4. *Chest X-ray* for tuberculosis or malignancy lung or lymphoma
5. *Lymph node biopsy* – if lymph node enlarged
6. *CSF examination*. Features of Froin's syndrome below the level of compression will be evident if spinal tumour is the cause of spinal block.
  - Low CSF pressure
  - Xanthochromia
  - Increased protein
  - Normal cellular count
  - Positive Queckensted test (i.e. no rise in CSF pressure following compression of internal jugular vein)

7. *CT myelography* to determine the site and type of compression. Now-a-days it has been replaced by MRI.

The CT myelography may show;

- i. *Meniscus sign* in intradural compression
- ii. *Brush border sign* in extradural tumours
- iii. *Candle-wax or Candle-guttering appearance* in arachnoiditis
- iv. *Expansion sign* in syringomyelia
8. *MRI* to find out the cause of compression
9. *Other tests* depending on the cause or disease.

**484. What is albumino-cytological dissociation?**

**Ans.** It refers to increased protein content in CSF with no parallel rise in cell count, hence, the word dissociation is used. The causes are:

- GB syndrome
- Froin's syndrome (spinal block due to a spinal tumour)
- Acoustic neurofibroma
- Cauda equina syndrome.

**485. What are causes of xanthochromia (yellow colouration of CSF)?**

**Ans.** Following are the causes:

- Old subarachnoid haemorrhage
- GB syndrome
- Froin's syndrome
- Acoustic neuroma
- Deep jaundice.

**486. What is tropical spastic paraplegia (HTLV-1 associated myelopathy)?**

**Ans.** It is common in females (3rd, 4th decades) associated with HTLV-1 infection where the patient develops gradual onset of weakness of legs (paraplegia) which progresses and patient becomes confined to wheel chair within 10 years. This is UMN spastic paraplegia without sensory disturbance. Bladder disturbance and constipation are common. This is an example of noncompressive progressive myelopathy. The diagnosis is suggested by seropositivity for HTLV-1.



**CASE 35: PERIPHERAL NEUROPATHY**

The patient (Fig. 1.35A) presented with following complaints:

1. Sensations of pins and needles (tingling and numbness) in the distal parts of all the four limbs
2. Weakness of all the limbs especially distal parts
3. Thinning of legs

**History—Points to be Noted**

- Note the duration and onset of symptoms
- Initiation and distribution of sensory disturbance (i.e. glove-stocking anaesthesia)
- Evolution of weakness (proximal or distal). Was there any difficulty in holding the things?
- Progression of symptoms, e.g. stationary, progressive, recovering or waxing and waning
- Is there any history of weakness of respiratory muscles or facial muscles. Difficulty in coughing or breathing?
- History of taking drugs (e.g. INH)
- Any precipitating factor or illness
- Bowel and bladder disturbance.

**Past History**

Ask for;

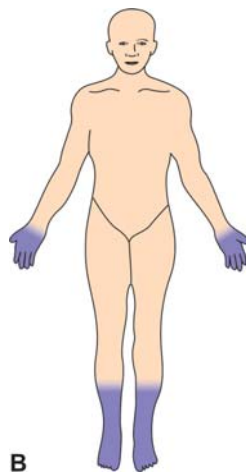
- Alcoholism
- Headache, vomiting, convulsions
- Diplopia, dysphagia, nasal regurgitation
- Past history of spinal trauma
- History of fever, contact with a patient of tuberculosis, exposure to STD, vaccination
- History of systemic illness, i.e. diabetes, renal failure, chronic liver disease, diarrhoea or malabsorption, etc.
- History of exposure to solvents, pesticides or heavy metals.

**Family History**

- History of similar illness in other family members.

**General Physical Examination**

- Consciousness and behaviour
- Look for anaemia, jaundice, oedema
- Look for signs of vitamin deficiencies i.e. tongue, eyes, mucous membranes
- Look for alcoholic stigmata, e.g. gynaecomastia, testicular atrophy, muscle wasting, parotid enlargement, palmar erythema or flushing of face. Look at the skin for hypopigmented or hyperpigmented patches, scar or burn mark
- Record pulse, BP and temperature



**Figs 1.35A and B:** Peripheral neuropathy. A. A patient with bilateral foot drop due to peripheral neuropathy. B. Glove-stocking type of anaesthesia (diagram).

**Systemic Examination (Read CNS Examination)**

- Higher functions
- Cranial nerves
- Neck rigidity

**Motor function**

- Look the posture (usually decubitus) and foot drop
- Note the nutrition, tone, power and coordination of the muscles
- Elicit the tendon jerks. Bilateral ankle jerks are usually absent

**Sensory system**

- Test superficial and deep sensations including cortical sensations. They are lost in the peripheral parts
- Palpate the various long nerves (ulnar, radial, common peroneal). They may be palpable in diabetes, leprosy, hereditary polyneuropathy

**Other system examination**

1. CVS for sounds, bruits and murmurs
2. Respiratory system for evidence of tuberculosis, sarcoidosis, malignancy
3. GI tract for hepatosplenomegaly
4. Lymphoreticular system for lymph node enlargement

**Clinical Presentations**

- These patients may present with acute onset of areflexi paralysis of all the four limbs called post-infective polyneuritis (Guillain-Barré syndrome)
- Chronic cases of peripheral neuropathy present with paraesthesias (tingling and numbness) of hands and feet with weakness and thinning of legs with or without wrist or foot drop

**487. What is clinical presentations of peripheral neuropathy? Name the terms used in relation to neuropathy?**

**Ans.** Clinical presentations are:

- Distal paraesthesias (pins and needles sensation) is the presenting symptom usually first affecting the feet and then the hands and subsequently progressing upwards but stopping short below the knees and elbows.
- Loss of all types of sensations in a glove-stocking distribution (Fig. 1.35B). Patient may be unaware of injury or burn marks on the hands in smokers and on the feet in labourers.
- Distal weakness of all the four limbs leading to bilateral foot drop and or/bilateral wrist drop.
- There may be autonomic disturbances in peripheral parts, i.e. postural oedema, cold extremities etc.

**Terminology Used in Relation to Neuropathy**

**Neuropathy** means a pathological process affecting a peripheral nerve or nerves

**Mononeuropathy** refers to a process affecting a single nerve (radial, ulnar, median, etc).

**Multiple mononeuropathy (mononeuritis multiplex)** refers to a process involving several or multiple long nerves.

**Polyneuropathy or peripheral neuropathy** refers to a diffuse symmetrical disease process involving the peripheral parts and progressing proximally.

**Radiculopathy** means a disease process affecting the nerve roots (motor or sensory).

**488. What are the causes of peripheral neuropathy?**

**Ans.** There are numerous causes of peripheral neuropathy, out of which some are common such as diabetes, toxins (alcohol or drug induced), Guillain-Barre syndrome, leprosy and chronic renal failure (Table 1.130).

**489. What are causes of acute onset peripheral neuropathy?**

**Ans.** Causes are:

- GB syndrome
- Diabetes mellitus
- Drugs (TOCP, Arsenic)
- Diphtheria
- Porphyria
- Paraneoplastic syndrome

**Table 1.130:** Aetiology of peripheral neuropathy

Type	Common	Uncommon	Rare
Metabolic/endocrinal	<ul style="list-style-type: none"> <li>• Diabetes</li> <li>• Chronic renal failure</li> <li>• Amyloidosis</li> <li>• Hypothyroidism</li> <li>• Liver cell failure</li> </ul>	<ul style="list-style-type: none"> <li>• Multiple myeloma</li> <li>• Cryoglobulinaemia</li> </ul>	Porphyria
Toxic	Alcohol induced	Drug induced (e.g. INH, vincristine, phenytoin, NFT)	Heavy metals (Pb, As, Hg) and organic solvents (TOCP)
Inflammatory or infective	Guillain-Barre syndrome	Chronic inflammatory demyelinating polyneuropathy, connective tissue diseases, e.g. SLE, PAN, Sjögren's syndrome and infective (leprosy diphtheria, typhoid fever, HIV)	Multiple motor neuropathy with conduction block
Genetic	—	Hereditary motor and sensory neuropathies (Charcot, Marie-Tooth)	Other hereditary neuropathies
Deficiency states	—	<ul style="list-style-type: none"> <li>• Vit. B<sub>1</sub> deficiency</li> <li>• Vit. B<sub>12</sub> deficiency</li> </ul>	Vit. A and E, pyridoxine deficiency
Others	—	Malignant disease (paraneoplastic neuropathy)	
	—	Critical illness neuropathy	

**490. What are the causes of predominant motor neuropathy?**

**Ans.** Causes are:

- G.B. syndrome (70%)
- Porphyria
- Connective tissue diseases, e.g. SLE, PAN
- Hereditary polyneuropathy
- Acute motor axonal neuropathy
- Delayed neurotoxicity due to organophosphates (TOCP, TCP)
- Diphtheria
- Lead intoxication
- Hypoglycaemia
- High doses of dapsone.

**491. What are the causes of pure sensory neuropathy?**

**Ans.** Causes are:

- Hereditary sensory neuropathy
- Paraneoplastic syndrome
- Leprosy
- HIV
- Thalidomide toxicity
- Pentamidine sensory neuropathy
- Cisplatin (antineoplastic)
- Sjögren's syndrome
- Dysproteinaemia

**492. What are the causes of recurrent neuropathy?**

**Ans.** These patients may have several attacks of neuropathy. The common causes are:

- Porphyria
- Chronic inflammatory demyelinating polyneuropathy (CIDP)
- Alcoholic neuropathy
- Occupational toxic neuropathy.

**493. What are the causes of peripheral neuropathies with predominant autonomic neuropathy?**

**Ans.** Most varieties of polyneuropathy affect autonomic functions to a mild extent, but certain neuropathies may have predominant autonomic dysfunction. The causes are;

- Diabetes mellitus

- Porphyria
- Alcoholism
- Leprosy
- Amyloidosis
- G.B. syndrome

**494. How do you classify neuropathy in diabetes mellitus?**

**Ans.** Neuropathy is a microvascular complication of diabetes, occur commonly in type 2 than in type 1 diabetes. It may be symmetric or asymmetric, motor, sensory or mixed (Table 1.131).

**Table 1.131:** Classification of diabetic neuropathy depending on distribution pattern

**1. Symmetric**

- a. Distal, primarily sensory polyneuropathy (mainly large fibre, small fibre or mixed type)
- b. Autonomic neuropathy
- c. Chronically evolving proximal motor neuropathy

**2. Asymmetric**

- a. Acute or subacute proximal motor neuropathy (diabetic amyotrophy)
- b. Cranial mononeuropathy (3rd and 6th cranial nerve involved)
- c. Truncal neuropathy
- d. Entrapment neuropathy in the limbs (ulnar, median nerve)

**495. How do you diagnose peripheral neuropathy?**

**Ans.** The diagnosis of peripheral neuropathy is based on the peripheral signs which are:

1. **Sensory loss of all modalities** in glove-stocking fashion in both upper and lower limbs, i.e.
  - Loss of sensations carried by spinothalamic tract, e.g. pain, temperature, crude touch
  - Loss of sensations carried by posterior column, e.g. vibration sense, joint position sense, deep pressure and fine touch
2. **Loss of motor functions, i.e.**
  - Wasting of small muscles of hands and feet.
  - Loss of deep peripheral jerks in lower limbs, e.g. ankle
  - Loss of deep peripheral jerks of upper limb, e.g. supinator and finger flexion
  - Bilateral wrist or foot drop.

3. **Autonomic dysfunction** (read features of autonomic neuropathy p. 120)
4. Confirmation of diagnosis is made by nerve conduction studies. Nerve conduction studies can distinguish demyelinating neuropathy from axonal neuropathy.

- In *demyelinating neuropathy*, there is slowing of conduction velocity, dispersion of evoked compound action potentials, conduction block and marked prolongation of distal latencies.
- In contrast in *axonal type*, there is reduction in amplitude of evoked compound action potentials with preservation of nerve conduction velocity.

**496. What are various symptoms of axonal and demyelinating neuropathies? What are their causes?**

**Ans.** The distinction between axonal and demyelinating polyneuropathy is mainly based on the electrophysiological studies. Both axonal and demyelinating neuropathies present in a similar manner, can be acute, subacute and chronic. The causes are given in Table 1.132.

**Table 1.132:** Major types of neuropathy (axonal vs demyelinating)

Type	Axonal	Demyelinating
Acute	Porphyria, toxic (As) GB syndrome	All forms of GB syndrome
Subacute	Toxic/metabolic	Relapsing form of CIDP
Chronic	Toxic or metabolic Hereditary Diabetic Dysproteinaemia	Hereditary Inflammatory Autoimmune Dysproteinaemia Toxic/metabolic

**497. What is differential diagnosis of polyneuropathy?**

**Ans.** The differential diagnosis lies between its various causes. The characteristics of some common causes of neuropathies are discussed here.

**1. Guillain-Barré Syndrome.** The characteristic features are:

- It is an acute, frequently severe and fulminant polyradiculopathy of autoimmune origin

- Peak incidence between 20-50 years
- It manifests as rapidly evolving areflexic (LMN type) motor paralysis with or without sensory disturbance
- It usually starts from the lower extremities followed by upper extremities or all the four limbs may be involved simultaneously (uncommon). The legs are more affected than arms
- The lower cranial nerves are also frequently involved, causing bulbar weakness. The VII cranial nerve is frequently involved producing LMN type of paralysis. Bilateral involvement is common though it can occur unilaterally.
- Deep tendon reflexes are diminished in the limbs
- Bowel and bladder are rarely involved
- Plantars are either flexor or not elicitable
- Sensorium is clear throughout the illness
- The usual variant is *Miller-Fischer syndrome* which comprises of a triad of ophthalmoplegia, ataxia and areflexia.

The diagnostic criteria are listed in Table 1.133.

**Table 1.133:** Diagnostic criteria for Guillain-Barré Syndrome

Essential	Supportive
<ul style="list-style-type: none"> <li>• Progressive weakness of 2 or more limbs due to neuropathy</li> <li>• Areflexia (loss of reflexes)</li> <li>• Disease course &lt;4 weeks</li> <li>• Exclusion of other causes of LMN type of paraplegia or quadriplegia</li> </ul>	<ul style="list-style-type: none"> <li>• Relative symmetric weakness</li> <li>• Mild sensory involvement</li> <li>• Facial and other cranial nerve involvement</li> <li>• Absence of fever</li> <li>• Typical CSF changes (acellularity, rise in protein)</li> <li>• Electrophysiologic evidence of demyelination</li> </ul>

**2. Diabetic peripheral neuropathy**

- History of diabetes, i.e. type I (polyuria, polydipsia or polyphagia) or type 2 (impaired wound healing, infections, etc.)
- History of intake of either insulin or OHA
- Duration of diabetes is longer
- A triad of retinopathy, neuropathy and nephropathy may occur but these complications can occur individually also

- History of susceptibility to infection, weakness, impaired wound healing
  - The various types of neuropathy in diabetes have already been described.
3. **Leprosy**
    - Typical 'Leonine' facies
    - Typical hypopigmented and anaesthetic skin lesions
    - Palpable peripheral nerves with peripheral neuropathy
    - Trophic changes
  4. **Diphtheric neuropathy**
    - Common in children, but now rarely observed due to effective immunisation against diphtheria
    - Palatal weakness followed by pupillary paralysis and sensorimotor neuropathy
    - Cranial nerves 3rd, 6th, 7th, 9th and 10th may be involved
    - The condition develops 2-6 weeks after the onset of disease
    - Myocarditis may occur in two-thirds of patients with diphtheria. It manifests on ECG as arrhythmias, conduction blocks, ST-T changes and CHF.
  5. **Prophyric neuropathy**
    - Acute intermittent porphyria produces attacks of paroxysmal neuropathy simulating G.B. syndrome
    - This is associated with abdominal colic, confusion, autonomic disturbances and later coma
    - Alcohol and barbiturates precipitate the attacks
  6. **Arsenical neuropathy**
    - Rain-drop skin lesions with hyperkeratosis of palms and soles
    - People of known geographical area using deep tube-well water are mainly affected
    - Mee's line (white transverse ridges on nails) are diagnostic
    - Presence of anaemia with or without jaundice (hepatic involvement)
    - Diagnosis is confirmed by estimation of arsenic in skin, nails, hair and urine
  7. **Neuropathies with HIV infection**
    - Distal, symmetric, mainly sensory polyneuropathy which evolves slowly in symptomatic HIV disease, is associated with encephalopathy and myelopathy
  - GB syndrome or chronic inflammatory demyelinating polyneuropathy (CIDP) may occur following conversion to seropositivity and during the asymptomatic phase of the disease.
  8. **Neoplastic neuropathy.** Polyneuropathy is sometimes seen as a non-metastatic manifestation of a malignancy (paraneoplastic syndrome) which may be motor or sensorimotor.
 

In multiple myeloma and other dysproteinaemias, the polyneuropathy occurs due to demyelination associated with allergic reaction within peripheral nerves. The POEMS syndrome is an example of polyneuropathy in multiple myeloma in which

P stands for chronic inflammatory demyelinating polyneuropathy

O stands for organomegaly (hepatomegaly)

E stands for endocrinopathy (gynaecomastia and atrophic testes)

M stands for M band on electrophoresis

S stands for skin pigmentation.
  9. **Hereditary neuropathy (Charcot-Marie-Tooth disease)**
    - An autosomal dominant/recessive/X-linked transmission. It occurs in first and second decades of life.
    - Sensorimotor neuropathy characterised by distal muscle weakness and atrophy, impaired sensations, absent or hypoactive deep tendon reflexes
    - Pattern of involvement is feet and legs followed by hands and forearm
    - High-steppage gait with frequent falling due to bilateral foot drop
    - Foot deformity (pes cavus, high arch feet) and hand deformity due to atrophy of intrinsic muscles of the hands.
  10. **Chronic inflammatory demyelinating polyneuropathy (CIDP)**
    - It is a chronic G.B. syndrome, affects young adults
    - Onset is gradual, sometimes subacute, and the initial episode is indistinguishable from that of GB syndrome



- It is a sensorimotor neuropathy with predominant motor findings, but a small number of patients may present with pure syndrome of sensory ataxia.
  - Some patients experience a chronic progressive course, whereas, others have a relapsing and remitting course.
  - Some patients may have cranial nerve involvement including external ophthalmoplegia
- The diagnosis is confirmed on typical CSF findings and electrophysiological studies which show findings similar to GB syndrome.

#### 11. **Triorthocresylphosphate (TOCP) neuropathy**

It is called '*ginger paralysis*' owing to consumption of fluid extract of ginger which was used in the manufacture of bootleg alcohol and was adulterated with TOCP. It is pure motor neuropathy characterised by bilateral foot and hand drop. It occurs 10-20 days after consumption of adulterated food (cooking - oil ) or drink.

#### **498. What are the causes of foot drop?**

**Ans.** Paralysis of extensors of foot and peronei muscles produces foot drop. The common causes are;

- Peripheral neuropathy (bilateral foot-drop)
- Common peroneal nerve palsy (unilateral foot-drop)
- PIVD (lesion involving L<sub>5</sub>) produces unilateral or bilateral foot drop
- Motor neuron disease (bilateral foot-drop)
- Sciatic nerve lesion (unilateral foot-drop)
- Peroneal muscle atrophy (bilateral foot-drop)

#### **499. What are the causes of wrist-drop?**

**Ans.** Paralysis of the extensors of wrist produces wrist-drop. The patient is not able to extend the wrist and fingers when asked to do so. In an attempted extension of fingers, there will be flexion of metacarpophalangeal joints and extension of the interphalangeal joints due to unopposed action of lumbricals and interossei.

#### **Causes**

- Radial nerve palsy
- Lead neuropathy
- Other peripheral neuropathies

#### **500. What are characteristics of root (radicular) lesion?**

**Ans.** Following are characteristics:

- Lesion of the anterior (motor) root(s) produces weakness and atrophy of the muscles innervated by these roots.
- Irritative lesion of posterior (sensory) root produces root pain (increases with coughing), hyperalgesia (calf tender on squeezing) or hyperaesthesia related to the segment irritated. In compressive lesion (radiculopathy), there is segmental sensory loss such as in PIVD or cauda equina syndrome (saddle-shape anaesthesia).

#### **501. What is mononeuritis? What are characteristics of various mononeuropathies?**

**Ans.** Involvement of a single nerve (mononeuritis) is either acute (compression) or chronic (entrapment). In both, the demyelination predominates, but some axonal degeneration also occurs.

Acute compression usually affects nerves which are superficially placed at some point/region (e.g. the common peroneal nerve at the head of fibula). Entrapment occurs when a nerve passes through a relatively narrow or tight anatomical compartment (e.g. carpal tunnel). These conditions are diagnosed by clinical features and confirmation is done by conduction studies and EMG.

The symptoms and signs of various mononeuropathies are given in Table 1.134.

#### **502. What are the causes of carpal tunnel syndrome (median nerve compression)?**

**Ans.** These are:

- Hypothyroidism or myxedema
- Diabetes mellitus
- Pregnancy
- Obesity
- Acromegaly
- Rheumatoid arthritis
- Idiopathic

#### **503. What do you understand by the term mononeuritis multiplex (multiple mononeuropathy)?**

**Ans.** Mononeuritis multiplex refers to simultaneous or sequential involvement of individual non-contiguous

**Table 1.134:** Symptoms and signs of mononeuropathies

<i>Nerve</i>	<i>Symptoms</i>	<i>Muscle weakness</i>	<i>Sensory loss</i>
<b>1. Upper extremities</b>			
<i>Median</i> (carpal tunnel syndrome)	Nocturnal pain and tingling sensations on the palm and fingers waking the patient from sleep. Pain may extend to arm and shoulder	Abductor pollicis brevis	Lateral palm and thumb, index, middle and half ring finger (radial three and half fingers)
<i>Ulnar</i>	Tingling on medial (ulnar) border of hand; wasting and weakness of hand muscles	All hand muscles except abductor pollicis brevis	Medial palm and little and half ring finger (one and half medial fingers)
<i>Radial</i>	Wrist drop, weakness of fingers extension and hand supination	Wrist and finger's extensors, and supinator	Dorsum of the thumb
<b>2. Lower extremities</b>			
<i>Common peroneal</i>	Foot-drop	Dorsiflexors and everter of foot	Nil or dorsum of foot
<i>Lateral cutaneous</i> (Meralgia paraesthetica)	Tingling and paraesthesia on lateral aspect of thigh	Nil	Lateral border of thigh
<i>Femoral</i> (L2-L4) (diabetic amyotrophy)	Hip flexion and knee extension difficult	Anterior thigh muscles and loss of knee jerk	Front of thigh and lateral aspect on the back of thigh
<i>Sciatic</i> (L4-S3)	Severe leg weakness below knee, flail foot and severe disability	Hamstring muscles, hip abductor and all muscles below knee	—
<i>Posterior tibial</i> (tarsal tunnel syndrome)	Pain and numbness of sole, weak toe flexors	Calf muscles, toe flexors and intrinsic foot muscles	—

nerve trunks either partially or completely evolving over days to years. Usually there is ischemia of long nerves due to vasculitis involving vasa nervosa which renders the nerves prone to mechanical compression. The causes are;

- Diabetes mellitus
- Leprosy
- Collagen vascular disorders
- Sarcoidosis
- Amyloidosis
- Malignancy
- Neurofibromatosis
- AIDS
- Hypereosinophilic syndrome
- Cryoglobulinaemia

#### **504. What are the causes of brachial plexus lesions? What are characteristic features of these lesions?**

**Ans.** Trauma or injury (stab or gun shot) is the commonest cause of damage to the brachial plexus. The injury commonly occurs during forced separation of head and shoulder, during a fall, or following excessive abduction of the arm. Other causes include invasion of the plexus by neoplasia involving cervical lymph nodes or pulmonary apex (Pancoast's tumour), compression of the thoracic outlet (cervical rib or a fibrous band) and damage due to radiation to the axillary area. One or more spinal nerves may be involved by lesion of the cervical spine such as Klippel-Feil syndrome, fusion of vertebrae, fracture dislocation, prolapsed intervertebral disc, caries spine or malignant deposits. The plexus may be damaged by stabs or gun-shot wounds, by fracture of clavicle and by dislocation of upper end of the humerus. The clinical signs of brachial plexus lesions are given in Table 1.135.

**Table 1.135:** Physical signs in brachial plexus lesions

<i>Location</i>	<i>Root(s) affected</i>	<i>Weakness of muscles</i>	<i>Sensory loss</i>
1. <i>Upper plexus (Erb's paralysis)</i>	C <sub>5</sub> (C <sub>6</sub> )	Biceps, deltoid, spinati, rhomboids, brachioradialis, triceps, serratus anterior. Biceps and supinator jerks are lost	Small area over deltoid
<b>Causes.</b> Indirect violence resulting in the nerve being torn by undue separation of head and shoulder, such as birth injury. In adults, it may occur during fall from a motor cycle on one side. Occasionally, it occurs following general anaesthesia in patients in whom, during the operation the arm has been held abducted and externally rotated			
2. <i>Lower plexus (Dejerine-Klumpke paralysis)</i>	T <sub>1</sub> (C <sub>8</sub> )	All small muscles of hand, claw hand (ulnar/wrist flexors)	Ulnar border of hand/forearm
<b>Causes:</b> Birth injury or may be produced by a fall during which patient tries to save himself by clutching something with the hand			
3. <i>Thoracic outlet syndrome (cervical rib or a fibrous band)</i>	C <sub>8</sub> /T <sub>1</sub>	Small muscles of hands, ulnar/forearm muscles	Ulnar border of hand/forearm (upper arm)

## SHORT/SPOT CASES

### CASE 36: CUSHING'S SYNDROME

The male patient (Fig. 1.36) presented with puffiness of face, headache and weight gain. Examination revealed moon face (plethoric face), hypertension, and oedema. There were truncal obesity and abdominal striae. His left lower limb was in plaster (visible) due to fracture.



Fig. 1.36: Cushing's syndrome

#### 505. What is your diagnosis? What are the causes of moon face?

**Ans.** The symptoms and signs suggests the diagnosis of Cushing's syndrome in the patient in picture which could be iatrogenic (steroid-induced) or due to disease (excess secretion of corticosteroids).

The moon face just implies rounded face due to oedema irrespective of its cause.

The causes of moon faces are:

- Cushing's syndrome/Cushing's disease
- Nephrotic syndrome (there is associated marked periorbital oedema producing boggy lower lids)
- Acute nephritic syndrome (periorbital oedema with narrowing of palpebral fissure).
- Hypothyroidism/cretinism (puffiness of face, thick skin, coarse facial features, large tongue, thick lips)
- Superior mediastinal compression syndrome (suffused face, prominent neck and facial veins)
- Angioneurotic oedema of face.

#### 506. What is differential diagnosis of moon face?

**Ans.** The characteristic features of the disorders producing moon face are:

#### 1. Cushing's syndrome

The characteristic features include;

- Moon face, obesity (truncal or centripetal), camel hump
- Weight gain, hypertension, oedema
- Cutaneous striae, easy bruising, back pain, muscle weakness, osteoporosis
- Acne, hirsutism, menstrual irregularity
- Emotional changes
- Pigmentation and hypokalaemic alkalosis
- Raised blood cortisol levels (loss of diurnal pattern), raised urinary excretion of 17-OH corticosteroid and dexamethasone suppression test will confirm the diagnosis

#### 2. Nephrotic syndrome

Read the features in clinical case discussion No. 18

#### 3. Nephritic syndrome (read case discussion no. 17)

#### 4. Myxoedema (Read case discussion no. 25)

#### 5. Superior mediastinal syndrome (read case discussion no. 64). The characteristic features are;

- Cough, dyspnoea, chest pain
- Engorged but nonpulsatile neck veins
- Puffiness of face or moon face, cyanosis
- Hoarseness of voice, Horner's syndrome, vocal cord paralysis
- Paralysis of hemidiaphragm

#### 6. Angioneurotic oedema

- Type I hypersensitivity reaction, commonly due to drugs, e.g. ACE inhibitor
- Diffuse swelling of the eyelids, face (moon face), lips, tongue, hands, genital or other parts of the body
- Associated with itching
- Congenital variety is due to C<sub>1</sub> esterase deficiency
- Wheezing, shortness of breath, headache, nausea, vomiting, arthralgia may occur as systemic manifestations
- Glottis may be involved producing suffocation
- The condition reverses with use of adrenaline, antihistamine and a steroid.

#### 507. What are common indications of steroid therapy?

**Ans.** The indications of steroids therapy depending on mechanisms of action are enlisted in Table 1.136.

**Table 1.136:** Actions and indications of steroid therapy

Action	Uses
<ul style="list-style-type: none"> <li>• Anti-inflammatory agents</li> <li>• Antiallergic agent</li> <li>• Antilymphocytic</li> <li>• Immunosuppressive</li> <li>• Antifibroblastic agent to prevent adhesions</li> <li>• As replacement therapy in its deficiency</li> <li>• To lower intracranial tension</li> <li>• As a diagnostic test to suppress raised levels of endogenous steroids</li> </ul>	<ul style="list-style-type: none"> <li>• Rheumatoid arthritis, acute rheumatic carditis</li> <li>• Allergic skin conditions (urticaria), anaphylactic shock, acute severe asthma</li> <li>• Acute lymphatic leukaemia</li> <li>• Nephrotic syndrome, SLE and other collagen vascular disorders, interstitial lung disease, in organ transplantation to prevent rejection</li> <li>• Used locally or systemically in joint disease, pericardial and pleural effusion</li> <li>• Addison's disease, Sheehan's syndrome</li> <li>• Cerebral oedema, CVA, benign raised intracranial tension</li> <li>• Dexamethasone or steroid suppression test</li> </ul>

**508. What are its contraindications?**

**Ans.** The 'check list' prior to use of steroids include;

- Presence of tuberculosis or other chronic infection
- Glucose intolerance or history of gestational diabetes or presence of diabetes
- History of peptic ulcer, gastritis or hematemesis or melena (positive occult blood in stool)
- Hypertension
- Osteoporosis or postmenopausal women
- Previous history of psychological disorders.

**509. What are side effects of steroids?**

**Ans.** Read Unit 3—Commonly used drugs.

**510. What is Cushing's disease?**

**Ans.** It is a disease state characterised by excessive secretion of ACTH from the anterior pituitary leading to bilateral adrenal hyperplasia and hypercortisol state (excessive steroid production).

**511. What are characteristics of Cushing's syndrome due to ectopic ACTH production?**

**Ans.** The features are:

- Acute onset of symptoms
- Hyperpigmentation
- Hypertension and oedema are more common
- Hypokalaemic alkalosis a characteristic feature
- The diagnosis is confirmed by markedly elevated ACTH level (> 300 ng/l)

**512. What is Nelson's syndrome?**

**Ans.** This is characterised by increased ACTH production, hyperpigmentation and erosion of sella turcica due to development of chromophobe adenoma in patients with Cushing's disease who have undergone bilateral adrenalectomy. This syndrome will not occur if pituitary has also been irradiated after bilateral adrenalectomy.

**513. How do you classify steroids?**

**Ans.** Read Unit 3, Commonly used drugs.

**514. How will you investigate a case with Cushing's syndrome?**

**Ans.** Investigations are:

1. Blood examination for eosinopenia and neutrophilia
2. Serum sodium (hypernatraemia), K<sup>+</sup> (hypokalaemia) and pH (alkalosis)
3. Urinary excretion of 17-hydroxycorticosteroids increased
4. Glucose tolerance test may show impaired tolerance or frank diabetes (seen <20% cases)
5. *X-ray skull and spine*: X-ray skull may show enlargement of pituitary fossa if a pituitary tumour is suspected to be the cause. X-ray spines may show cord-fish vertebrae or fish-mouth appearance of intervertebral disc spaces
6. CT scan abdomen for adrenals may show a adrenal mass (adenoma or carcinoma) if adrenal is the cause
7. *Plasma cortisol level elevated*: There is loss of circadian rhythm
8. *Plasma ACTH levels*: They are high in ectopic ACTH production by a nonpituitary tumour, may be normal to high in pituitary tumour
9. *Dexamethasone suppression test*: There is no suppression of cortisol secretion in Cushing's syndrome
10. *Metyrapone test*: It differentiates between ACTH dependent Cushing's disease (exaggerated response) and non-ACTH dependent Cushing syndrome (no response)



**515. Name the abdominal striae.**

**Ans.** The striae are named as follows:

- Silvery white striae/striae gravidarum due to pregnancy or following delivery.
- Pink striae due to Cushing's syndrome or steroid excess.

**516. What is Conn's syndrome? What are differences between primary and secondary hyperaldosteronism?**

**Ans.** Conn's syndrome is primary hyperaldosteronism due to adenoma or hyperplasia of adrenal cortex or idiopathic in origin.

Secondary hyperaldosteronism means raised aldosterone levels due to oedematous states or low sodium such as seen in nephrotic syndrome, cirrhosis of the liver and congestive heart failure.

The differences between the two are given in the Table 1.137.

**Table 1.137:** Distinction between primary and secondary hyperaldosteronism

Primary hyperaldosteronism	Secondary hyperaldosteronism
<ul style="list-style-type: none"> <li>• It is due to involvement of adrenal cortex</li> <li>• Hypertension is a characteristic feature</li> <li>• Hypokalaemia is a characteristic feature with all its symptoms and signs</li> <li>• Plasma aldosterone levels elevated but renin activity is suppressed</li> </ul>	<ul style="list-style-type: none"> <li>It is secondary to oedematous states or low sodium</li> <li>No hypertension</li> <li>Hypokalaemia occurs, commonly due to use of diuretics</li> <li>Plasma aldosterone and plasma renin activity elevated</li> </ul>

**517. What is normal serum K<sup>+</sup> level? What are the causes of hypokalaemia?**

**Ans.** Normal serum K<sup>+</sup> level is 3.5 to 5.5 mEq/L. Hypokalaemia is said to be present when serum K<sup>+</sup> is <3.0 mEq/L. The common causes are;

1. Diuretics
2. GI tract diseases, e.g. diarrhoea or malabsorption
3. Metabolic alkalosis
4. Renal tubular acidosis

5. Deficient dietary intake
6. Cushing's syndrome
7. Conn's syndrome
8. Bartter's syndrome
9. Insulin effect as well as diabetic ketoacidosis.

**518. What are characteristic features of hypokalaemia?**

**Ans.** These are;

I. *Neuromuscular*

- Muscle weakness, fatigue
- Abdominal distension, adynamic ileus
- Distension of bladder, constipation
- Hyporeflexia

II. *Renal*

Metabolic alkalosis

III. *Cardiac*

- ECG changes, e.g. appearance of U waves, prolonged QTc, ST depression and T wave inversion
- Arrhythmias, e.g. ectopics, torsade de pointes.

**519. What is the pathogenesis of truncal obesity in Cushing's syndrome?**

**Ans.** It is due to redistribution of fat to central part under the effect of glucocorticoids.

**520. Name the hormones secreted by adrenal cortex and their effects.**

**Ans.** The hormones secreted and their effects are tabulated (Table 1.138).

**521. What are endocrinal causes of obesity?**

**Ans.** Cushing syndrome

- Hypothyroidism
- Hypogonadism (e.g. Frohlich's syndrome, Laurence-Moon-Biedl syndrome, Prader-Willi syndrome)
- Type 2 diabetes
- Following pregnancy and postpartum.

**522. What is android and gynoid obesity? What is their significance?**

**Ans.** Android obesity (e.g. abdominal or central obesity) is due to collection of fat in the abdomen above the waist producing apple-shaped body. It is associated with increased risk of CHD, HT, DM and dyslipidaemia.

Gynoid obesity is due to collection of fat below the waist i.e. on the hips and buttocks producing pear-shaped body. It predisposed the individual to mechanical complications, e.g. OA, varicose veins etc.

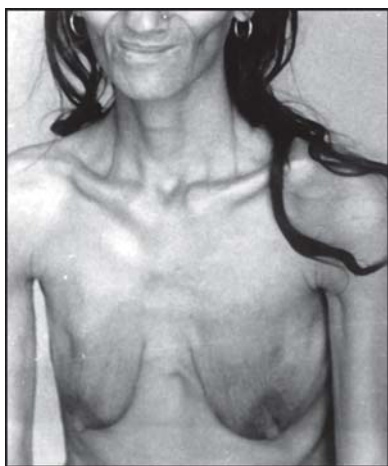
**Table 1.138:** Adrenocortical hormones

<i>Hormone</i>	<i>Effect</i>	<i>Symptoms and signs</i>
1. Aldosterone (mineralo-corticoid)	Retention of Na <sup>+</sup> and H <sub>2</sub> O	Oedema, hypertension, weight gain
2. Glucocorticoids	Redistribution of fat  • Mobilisation of proteins from supportive tissues, e.g. subcutaneous, bone and muscles • CNS effects  • ↑ ACTH in Cushing's disease	Truncal obesity, moon faces, camel hump  • Striae • Easy bruising • Back pain, fracture, osteoporosis • Emotional changes and personality changes • Pigmentation • Hypokalaemic alkalosis
3. Adrenal androgens	Virilisation	• Hirsutism and menstrual irregularity

**CASE 37: ADDISON'S DISEASE**

Figure 1.37 depicts features of Addison's disease.

The female patient presented with weakness, weight loss and pigmentation of face, buccal mucosa and palms. There is history of diarrhoea off and on. BP was 80/60 mmHg. The clinical findings of the patient are depicted in Figure 1.37.



**Fig. 1.37:** Addison's disease. A young female presented with shrunken cheeks, breast atrophy following postpartum bleeding (Sheehan syndrome—postpartum pituitary necrosis)

**523. What is your clinical diagnosis?**

**Ans.** The symptom triad of weakness, weight loss (glucocorticoids insufficiency), hypotension (mineralocorticoids insufficiency) and pigmentation of face and other sun-exposed areas (ACTH excess) suggests the diagnosis of Addison's disease.

**524. What are the causes of Addison's disease?**

**Ans.** The causes are:

**I. Common**

- Autoimmune (90%)
- Congenital adrenal hyperplasia
- Pituitary necrosis (Sheehan's syndrome)
- MEN Type I, II syndromes
- Tuberculosis, fungal infections (histoplasmosis, coccidioidomycosis, etc.) involving adrenals
- Bilateral adrenalectomy

**II. Rare**

- Metastatic tumours (bilateral)
- Amyloidosis, sarcoidosis
- Waterhouse-Friderichsen's syndrome (adrenal haemorrhage in meningococcaemia), HIV disease

- Hemochromatosis
- Adrenal infarction

**525. What is primary or secondary Addison's disease? How do they differ?**

**Ans.** Primary Addison's disease indicates adrenal involvement with high ACTH level due to feedback mechanism.

Secondary Addison's disease means involvement of either pituitary or hypothalamus with decreased ACTH levels.

The differences are given in the Box 1.3.

**Box 1.3:** Differences between primary and secondary Addison's disease

Primary	Secondary
<ul style="list-style-type: none"> <li>• Adrenal cortex is involved</li> <li>• Glucocorticoids, mineralocorticoids and androgens are low but ACTH is high</li> <li>• Pigmentation is common</li> </ul>	<ul style="list-style-type: none"> <li>Either pituitary or hypothalamus involved</li> <li>All the three hormones secreted by the adrenal cortex are low along with ACTH</li> <li>Pigmentation is rare</li> </ul>

**526. What are MEN Type I and MEN Type II syndromes?**

**Ans.** MEN means multiple endocrinal neoplasia causing syndromes of hormone excess.

*MEN Type I* (Werner's syndrome). It is characterised by neoplasia of parathyroid, pituitary and pancreatic islet cells.

*MEN Type II* (Medullary thyroid carcinoma, pheochromocytoma plus other neoplasia)

*A (Sipple syndrome)*: It consists of medullary thyroid carcinoma, pheochromocytoma, parathyroid adenoma.

*B (Mucosal neuroma syndrome)*: It includes medullary thyroid carcinoma, pheochromocytoma, mucosal and gastrointestinal neuromas, marfanoid features.

**527. What is adrenal crisis? What are its causes?**

**Ans.** The rapid and overwhelming intensification of chronic adrenal insufficiency usually precipitated by stress or sepsis is called *adrenal crisis*. Alternatively, acute adrenal insufficiency means acute involvement of bilateral adrenal glands in previously healthy subjects.

The causes are;

1. Septicaemia with pseudomonas or meningococcaemia (Waterhouse-Friderichsen syndrome)
2. Coagulation defect or anticoagulant therapy
3. Birth trauma in newborn
4. Idiopathic adrenal vein thrombosis or following venography
5. Sudden withdrawal of steroids in a patient with adrenal atrophy owing to chronic steroid administration.
6. Congenital adrenal hyperplasia or those with poor adrenal reserve precipitated by steroid synthesis inhibiting drugs (Ketoconazole).

### 528. How will you treat Adrenal crisis? (Read Emergency Medicine by Dr SN Chugh)

**Ans.** Treatment is as follows;

- Find out the cause or precipitating factor and remove or treat it appropriately.
- Replacement of glucocorticoids. Intravenous hydrocortisone (100 mg bolus) followed by continuous infusion of 10 mg/hr. Alternatively 100 mg bolus IV followed by same dose after every 6 hours.
- Replacement of sodium and water deficit by 5% glucose in normal saline solution. If patient has dehydration, several litres of saline solution may be infused over few hours.
- Treatment of hypotension: Replacement of fluid, sodium and glucocorticoids is sufficient to treat hypotension. Dopamine/ dobutamine infusion may be indicated as an adjunct to volume depletion in severe cases.
- Once patient is stabilised, steroids dosage is tapered over next few days to maintenance doses orally.

### 529. How will you diagnose Addison's disease?

**Ans.** The diagnosis depends on clinical features and investigations. The clinical suspicion arises when patient presents with hypotension with

- Weight loss, malaise, nausea, vomiting, weakness
- Diarrhoea—painless and progressive
- Pigmentation of sun-exposed areas, elbow, knees, creases of palm, knuckles, mucous membrane of the mouth, scars, etc.

The diagnosis is confirmed on investigations (Box 1.4).

### Box 1.4: Investigations for Addison's disease

Test	Primary Addison's	Secondary Addison's
1. Basal plasma cortisol levels e.g. morning and evening	Low	Low
2. ACTH	High	Low
3. ACTH stimulation test	Cortisol level does not rise	Subnormal rise
4. Serum Na <sup>+</sup>	Low	Low
5. Serum K <sup>+</sup>	High	Normal to high
6. Plasma glucose	Normal to low in severe disease	Normal
7. Aldosterone level	Low	Low to normal

### 530. What are the common conditions associated with hypotension?

**Ans.** The common conditions are

#### I. Hypovolaemia

- Excessive blood loss, e.g. external or internal haemorrhage, ruptured ectopic pregnancy, etc
- Excessive fluid loss, e.g. vomiting, diarrhoea, burns, diabetes mellitus or insipidous or diuresis and internal sequestration of fluid (e.g. peritonitis, pancreatitis, intestinal obstruction)

#### II. Hypotension due to cardiac origin

Acute MI, arrhythmias, myocarditis, rupture of interventricular septum, acute aortic regurgitation or dissection and myocardial depression due to drugs

#### III. Hypotension due to vasodilation

Septic shock, neurogenic shock, anaphylaxis, drug-induced (e.g. nitrates Ca<sup>++</sup> channel blockers, ganglion blockers, postural hypotension)

#### IV. Extra cardiac obstructive shock/hypotension

- Pericardial effusion, constrictive pericarditis, pulmonary embolism, coarctation of aorta

#### V. Miscellaneous

- Thyroid crisis, myxoedema coma, Addison's disease, cyanide and CO poisoning and endotoxaemia.

**CASE 38: TETANY**

The patient is 30 years female who presented with weakness, weight loss, intermittent muscle spasms especially involving the hands, feet and face. While taking the BP, the patient developed carpal spasms as shown in Figure 1.38.



**Fig. 1.38A:** Tetany. A patient with hypoparathyroidism showing provoked carpo-pedal spasms (Trousseau's sign)



**Fig. 1.38B:** Spontaneous carpopedal spasm in tetany. Note the main D' accoucher's or obstetrician's hand

**531. What is your diagnosis?**

**Ans.** In view of induced carpopedal spasm (Trousseau's sign) as well as history of muscle spasms, the patient appears to have tetany.

**532. Name the position of the hand.**

**Ans.** It is called obstetrician's hand or D' accoucher's hand.

**Table 1.139:** Causes of hypocalcaemia

**A. PTH absent**

- i. Hereditary hypoparathyroidism- DiGeorge syndrome (a rare disorder), Candidiasis endocrinopathy associated with familial autoimmune polyglandular deficiency syndrome
- ii. Acquired hypoparathyroidism, e.g. following surgical removal or irradiation damage
- iii. Hypomagnesaemia due to any cause

**B. PTH ineffective**

- i. Chronic renal failure
- ii. Vit. D deficiency, e.g. rickets, osteomalacia, drug induced (phenytoin)
- iii. Vit. D resistance
  - Vit. D resistant rickets (type II)
  - Intestinal malabsorption
- iv. Pseudohypoparathyroidism, e.g. Albright syndrome (short stature, round face, brachydactyly and heterotopic calcification)

**C. PTH overwhelmed**

- i. Severe, acute hyperphosphataemia
  - Tumour lysis
  - Acute renal failure
  - Rhabdomyolysis
- ii. Osteitis fibrosa cystica following parathyroidectomy

**533. What are the causes of hypocalcaemia?**

**Ans.** The functional classification of hypocalcaemia based on the mechanisms of production is tabulated (Table 1.139). The parathormone (PTH) is responsible for minute-to-minute regulation of plasma calcium. Therefore, hypocalcaemia can only occur when there is failure of homeostatic action of PTH. Failure of PTH response can occur due to:

- i. Hereditary or acquired parathyroid gland failure
- ii. PTH is either ineffective in target organs or its action is overwhelmed by the loss of calcium from the extracellular fluid at a rate faster than it can be replaced leading to hypocalcaemia.

**534. Name the common clinical conditions associated with chronic hypocalcaemia.**

**Ans.**

1. Hypoparathyroidism or pseudohypoparathyroidism
2. Rickets, osteomalacia (vit. D deficiency)
3. Chronic renal failure
4. Chronic diarrhoea, malabsorption syndrome
5. **Hyperphosphataemia** due to any cause, e.g. tumour lysis, ARF
6. Acute pancreatitis



**535. What are causes of transient hypocalcaemia?**

**Ans.** Transient hypocalcaemia does not produce tetany, occurs due to;

- Severe sepsis
- Burns
- ARF
- Repeated transfusions with citrated blood
- Medications such as protamine, heparin dilantin and glucagon.

**536. Does the low calcium levels are always associated with tetany?**

**Ans.** No. Total low calcium is not associated with tetany because ionised calcium may be normal in such a case. Low ionised calcium irrespective of calcium levels is associated with tetany. Transient hypocalcaemia is also asymptomatic, i.e. does not produce tetany.

**537. What are the causes of tetany?**

**Ans.** Tetany could be hypocalcaemic, hypomagnesaemic or alkalotic. Every hypocalcaemia is not associated with tetany. The low levels of ionised calcium with or without low total calcium lead to tetany (neuromuscular excitability). Idiopathic normocalcaemic tetany, spasmophilia occurs in both hereditary and acquired forms. The causes of tetany are given in Table 1.140.

**Table 1.140:** Causes of tetany  
(low ionised  $\text{Ca}^{++}$  <1.1 mmol/h or 4.5 mg%)

**I. Hypocalcaemia**

- Malabsorption
- Rickets and osteomalacia
- Hypoparathyroidism
- Chronic renal failure (usually tetany is prevented by acidosis)
- Acute pancreatitis
- Drugs, e.g. dilantin

**II. Hypomagnesaemia****III. Alkalosis and hypokalaemia**

- Repeated prolonged vomiting
- Excessive intake of alkali
- Hysterical hyperventilation
- Primary hyperaldosteronism
- Acute anion load

**538. What is normal serum calcium level?**

**Ans.** Normal level is:

- Total plasma calcium is 2.2 to 2.6 mmol/L (9-10.5 mg/dl)
- Ionised calcium is 1.1-1.4 mmol/L (4.5 to 5.6 mg/dl)

Usually hypocalcaemia is said to be present when serum calcium is <8.5 mg/dl. On the other hand, hypercalcaemia is said to present when calcium is >11.0 mg/dl.

**539. What are clinical features of hypoparathyroidism?**

**Ans.** Hypoparathyroidism is characterised by low calcium and high phosphate level either due to deficient production of parathormone (PTH) or its unresponsiveness. The clinical features are:

- Tetany
- Cataract
- Psychosis
- Basal ganglia calcification
- Epilepsy
- Papilloedema
- Candidiasis of nails, skin and mucous membrane may be associated with endocrinopathy–candida endocrinopathy.

**540. What are clinical features of tetany?**

**Ans.** Tetany may be latent or manifest. In manifest tetany, symptoms and signs depend on the age of the patient.

In children a characteristic triad of *carpopedal spasm*, *stridor* (loud sound due to closure of glottis) and *convulsions* may occur in various combinations. The hands in carpopedal spasms adopt a peculiar posture in which there is flexion at metacarpophalangeal joints and extension at the interphalangeal joints and there is apposition of thumb (main D'accoucher hand – see the Figure 1.38. Pedal spasms are less frequent.

- In adults. Tingling sensations (paresthesias) around the mouth and in the hands and feet are common. Carpopedal spasms are less frequent. Stridor and convulsions are rare.

**541. What is latent tetany?**

**Ans.** The absence of symptoms and signs of tetany in a patient with hypocalcaemia is called *latent tetany*. The tetany becomes manifest on provocative tests.

- Trousseau's sign (see Fig. 1.38A). Raising the BP above systolic level by inflation of sphygmomanometer cuff produces characteristic carpal spasms within 3-5 minutes
- Chvostek's sign. A tap at facial nerve at the angle of jaw produces twitching of facial muscles.

**542. How do you classify hypoparathyroidism?**

**Ans.** It is classified as either true (idiopathic) or pseudohypoparathyroidism.

**Table 1.141:** Distinguishing features between idiopathic hypoparathyroidism and pseudohypoparathyroidism

Idiopathic hypoparathyroidism	Pseudohypoparathyroidism
<ul style="list-style-type: none"> <li>• Usually acquired</li> <li>• PTH levels are low</li> <li>• Autoimmunity plays a role in some cases</li> <li>• Besides tetany, other features include epilepsy, psychosis, cataract, calcification of basal ganglia and papilloedema</li> </ul>	<ul style="list-style-type: none"> <li>• Congenital</li> <li>• PTH levels are high</li> <li>• Non- responsiveness to PTH either due to receptor or post-receptor defect</li> <li>• Besides tetany, other features include skeletal and developmental abnormalities such as short stature, short 4th and 5th metacarpal or metatarsals (brachydactyly) etc. called <i>Albright syndrome</i> or <i>Albright's hereditary osteodystrophy</i></li> </ul>

1. *True or idiopathic hypoparathyroidism* is due to deficient production of PTH. The symptoms and signs of hypoparathyroidism are present.

2. *Pseudohypoparathyroidism*. It is a heritable or congenital disorder characterised by tissue resistance to the effects of PTH.

In pseudohypoparathyroidism, in addition to symptoms and signs of hypoparathyroidism, there are distinct skeletal and developmental defects- a characteristic phenotype termed as Albright 'hereditary osteodystrophy.'

3. *Pseudopseudohypoparathyroidism*. A familial disorders in which skeletal and developmental defect are present without signs of hypoparathyroidism. PTH level is normal but there is resistance to its effects.

#### 543. What are differences between true and pseudohypoparathyroidism?

**Ans.** Table 1.141 presents differentiating features between both.

#### 544. How will you treat tetany?

**Ans.** The steps of treatment are:

1. Treatment of hypocalcaemia by calcium gluconate (10% 20 ml IM or IV) followed by oral supple-

mentation of calcium and vitamin D analogue. If not relieved by calcium, potassium and magnesium may be tried.

#### 2. Treatment of alkalosis

- Withdraw the alkalies if it has been the cause
- Isotonic saline IV if vomiting is the cause
- Inhalation of 5% CO<sub>2</sub> in oxygen if hyperventilation is the cause
- Psychotherapy for hysterical hyperventilation

#### 545. What is the effect of hypocalcaemia on ECG?

**Ans.** There is prolongation of QT (QT<sub>c</sub>) interval which may predispose to arrhythmias similar to hypokalaemia.

#### 546. How does hyperventilation lead to tetany?

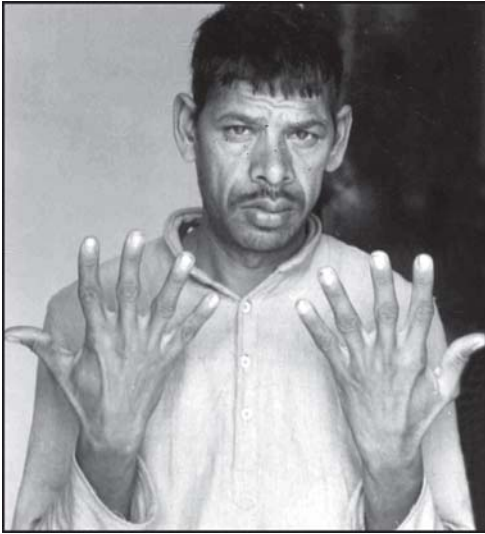
**Ans.** Hyperventilation occurring frequently or if prolonged leads to tetany by producing alkalosis due to washing out of CO<sub>2</sub>.

#### 547. Why does hypocalcaemia in CRF does not lead to tetany?

**Ans.** Hypocalcaemia in CRF is common but tetany is rare. It is due to the fact that ionised calcium does not fall to such a level to produce tetany because of associated metabolic acidosis in patients with CRF.

**CASE 39: ACROMEGALY**

The patient presented with coarse facial features and short stubby fingers and large hands (Fig. 1.39). There was associated hypertension.



**Fig. 1.39:** A patient with acromegaly. Note the stout built, broad, short stubby fingers and spade like hands

**548. What is the clinical diagnosis?**

**Ans.** The coarse facial features, thick skin, short fingers, large hands and stout built with hypertension indicate excess of growth hormone (GH) in the adult male – a condition called *acromegaly*. Thus, this patient is acromegalic male.

**549. What is the commonest cause of this condition?**

**Ans.** A pituitary tumour mostly a GH secreting adenoma is the commonest cause ( $\geq 60\%$  of cases). Prolactinoma is the second common cause.

**550. What are the clinical features of acromegaly?**

**Ans.** Clinical features of acromegaly depicted in Table 1.142).

**551. What are the disorders of GH?**

**Ans.** The disorders of GH are due to its excess or deficiency.

**1. Disorders due to excess of GH**

- Gigantism in adolescents. It is due to excess of GH before fusion of epiphysis
- Acromegaly in adults. It is due to excess of GH after fusion of epiphysis leading to enlargement of acral parts, hence, its name (*Acral* means distal, *megaly* means large)

**2. Disorders due to deficiency of GH.**

- Dwarfism (short stature)

**552. What are the neurological manifestations in Acromegaly?**

**Ans.** Neurological manifestations are as follows:

**A. Cranial nerve palsy**

1. Optic nerve. Pressure on the optic chiasma leads to bitemporal hemianopia (commonest), compression of optic nerve will lead to blindness due to optic atrophy.

**Table 1.142:** Clinical features of acromegaly

System/organ	Symptoms and signs
General	Normal height, stout and stocky built
Skin	Thickening, excessive perspiration, acanthosis nigricans
Soft tissues	Thick lips, macroglossia, thick nose, increase in heel pad ( $>22$ mm)
Viscera	Visceromegaly (e.g. liver, spleen, heart, tongue)
Joints	Arthropathy
Muscles	Myopathy
Acral parts (hands and feet)	Spade like hands, thick short and stubby fingers, large feet with increase in the size of shoes, carpal tunnel syndrome (compression of median nerve)
Skull	Prominent ridges and furrows
Jaws	Prognathism (protuding lower jaw)
Sinuses	Large frontal and maxillary sinuses
Eyes	Visual field defects, e.g. bitemporal hemianopia or scotomas
Others	Hypertension, galactorrhoea in females

**Table 1.143:** GH producing tumour

Tests	Results
Basal GH level	High
Prolactin level	High (in 30%)
Glucose tolerance suppression test by 75 g glucose	There is either no suppression or paradoxical rise of GH
X-ray skull for pituitary fossa	There may be enlargement of pituitary fossa with destruction of clinoid processes
X-ray heel pad thickness	Increased (>22 mm)
X-ray sinuses	Large and widened sinuses
Visual fields	Bitemporal hemianopia or scotoma
CT scan	A small or large hypodense microadenoma may be seen

2. Paralysis of 3rd, 4th and 6th nerves leads to external ophthalmoplegia.
3. VIIIth nerve involvement leads to deafness.

**B. Peripheral nerve compression**

- Carpal tunnel syndrome (median nerve compression).

**553. What are causes of carpal tunnel syndrome? What are its characteristic features?**

**Ans.** Following are the causes:

- Myxoedema
- Pregnancy
- Acromegaly
- Amyloidosis (primary)
- Rheumatoid arthritis
- Diabetes mellitus
- Compression of median nerve due to oedema, tenosynovitis, fascitis, fracture etc.
- Osteoarthritis (rare)
- Exposure to excessive vibration, seen in tractor drivers, mobile crane drivers and in workers involved in grinding using drills.
- Idiopathic

It produces median nerve compression, hence leads to:

- Pain, paraesthesias and numbness in the hand involved
- Weakness of abductor pollicis brevis
- Tapping over the median nerve at carpal tunnel produces paraesthesias along the cutaneous distribution of the nerve (**Tinel's sign**)

**554. How can you assess activity in acromegaly?**

**Ans.** Acromegaly is assessed for its activity as follows;

- Increasing sizes of the gloves, rings and shoes
- Ill-fitting of previous dentures
- Excessive perspiration and increasing headache
- Increasing visual loss
- Excessive sebum production
- Serial photographs of the patient may reveal progressive macrosomia
- Biochemical evidence of raised GH and somatomedin C levels

**555. How will you investigate such a patient?**

**Ans.** The investigations and the test results of a GH secreting tumour are listed in Table 1.143.

**556. What is treatment of acromegaly?**

**Ans.** Following are treatment methods:

1. **Medical:** Bromocriptine, a long-acting dopamine agonist may be used to lower the GH levels in active disease. The dose is 15-30 mg/day in divided doses; starting at a low dose of 2.5 mg/day and then gradually increasing it. Side effects include nausea, vomiting, postural hypotension, constipation and dyskinesia.

Now-a-days a somatostatin analogue, i.e. octreotide is used subcutaneously three times a day.

2. **Surgical:** Surgical treatment is indicated for pituitary tumours with compressive symptoms. Removal of adenoma by trans-sphenoidal route is preferred mode of surgery.
3. **Radiotherapy:** Pituitary is irradiated externally by gamma rays or by accelerated proton beam (linear accelerator) or internally by implanting rods of yttrium (radioactive isotope) into the pituitary gland.

**CASE 40: DWARFISM**

An 18-year-old female presented with short stature, decreased weight and failure of development of secondary sexual characters and menstrual irregularity (Fig. 1.40A).



**Fig. 1.40:** Pituitary dwarfism. An 18-year-old female pituitary dwarf (A) compared with age and sex match control (B)

**557. What is your clinical diagnosis?**

**Ans.** The patient appears to be dwarf, the cause of which appears to be endocrinal, i.e. hypopituitarism.

**558. How do you define dwarfism and short stature?**

**Ans.** Dwarfism means short stature where the height of person is much below the prescribed normal height in relation to his/her chronological age and sex. Short stature is defined as height of the child  $>2.5$  SD below the mean for chronological age, or the growth velocity that falls below 5th percentile on the growth velocity curve. Dwarfism means height below 3rd percentile of normal population of same age and sex.

**559. What are the causes of short stature?**

**Ans.** Causes of short stature are:

1. Heredofamilial
2. Constitutional delayed growth
3. Idiopathic
4. Skeletal dysplasias and rickets

5. *Dysmorphic syndromes*

- Noonan syndrome
- Down's syndrome
- Turner's syndrome
- Russel-Silver syndrome

6. *Nutritional*

- Coeliac disease
- Inflammatory bowel disease
- Poor diet intake and food faddism

7. *Chronic illnesses*

- Chronic infections
- Chronic renal failure
- Thalassaemia major

8. *Endocrinopathies*

- Isolated GH deficiency
- Hypothyroidism (cretinism)
- Hypopituitarism
- Cushing's syndrome
- Pseudohypoparathyroidism
- Uncontrolled type I diabetes

9. *Intrauterine growth retardation***560. Significance of history taking in a case with short stature.**

**Ans.** The natal (prenatal, intranatal and postnatal) history, the family and personal history are important.

1. *Prenatal history:* Ascertain the followings:

- Age of mother at conception
- Exposure to smoking and alcohol
- TORCH infection (Toxoplasma, Rubella, CMV, Herpes)
- Exposure to irradiation
- Any chronic illness during pregnancy
- Any thyroid disorder during pregnancy
- Exposure to drug-phenytoin

2. *Intranatal*

- Duration of gestation, e.g. premature delivery
- Nature of delivery, e.g. vaginal, forceps used or caesarean section
- Birth weight
- Birth asphyxia, cry after birth
- Persistence of neonatal jaundice

3. *Postnatal*

- Development of milestones



**Table 1.144:** Differential conditions for short stature

<i>Causes</i>	<i>Clinical features</i>
GH deficiency	Chubby child, frontal bossing, central obesity, high pitched voice, midline defects
Hypothyroidism (cretinism)	Read the clinical features as a separate question
Cushing's syndrome	Moon face, central obesity, striae, hypertension, camel hump, hirsutism
Pseudohypoparathyroidism	Moon facies and obesity, short metacarpals and metatarsals, mental retardation, tetany, epileptic convulsions, basal ganglia calcification
Rickets	Craniotables, widened wrist joint, rickety rosary, Harrison's sulcus, genu valgum, scoliosis, lordosis, kyphosis, protuberant abdomen
Down syndrome (Trisomy 21)	Read the clinical features of Down's syndrome – separate question
Noonan syndrome	Phenotype characteristics of Turner's syndrome, microphallus and delayed puberty are common
Achondroplasia (premature fusion of epiphyses)	Normal mental and sexual development, short limbs, large head with saddle nose, lumbar lordosis or kyphoscoliosis. They are seen as jokers in circus.
Prader-Willi syndrome	Hypotonia, obesity, hypogonadism, mental deficiency, small hands and feet with growth retardation
Laurence-Moon-Biedl syndrome	Obesity, hypogonadism, mental retardation, polydactyly and retinitis pigmentosa

- Height gain in a year
- History of chronic or recurrent illness

4. *Family history*

- Parent's height, e.g. mother and father
- Height of the siblings
- Any family history of growth delay
- Constitutional growth delay

5. *Personal history*

- Dietary history – caloric intake, food faddism
- Protein and calcium intake
- Scholastic performance
- Relationship with peers

**561. What is differential diagnosis of short stature?**

**Ans.** The conditions and their clinical features associated with short stature are enlisted in Table 1.144.

**562. What is Down's syndrome? What are its characteristic features?**

**Ans.** Down's syndrome is a chromosomal disorder characterised by trisomy 21 (chromosome 21 is present in triplicate) as a result of nondysjunction during meiosis.

The characteristic features are:

1. *Mongol facies (mongolism)*

- Microcephaly
- Upward slanting eyes with epicanthical folds
- Small, low-set ears

- Depressed bridge of the small nose
- Widely-set eyes (hypertelorism)
- Open mouth, fissured protruding tongue (macroglossia)
- High arched palate and small teeth
- Idiotic face

2. *Short and broad hands (Simian hand)*

The hands have

- Single palmar crease (simian crease)
- Clinodactyly (hypoplasia of middle phalanx of little finger resulting in incurving of it)
- Missing of one crease in little finger

3. *The feet show;*

- *Sandle gap*, e.g. increased gap between first and second toe
- Single longitudinal crease in the sole

4. *The eyes show;*

- Brushfield's spot
- Cataract
- Squint

5. *CVS*

- Endocardial cushion defects (e.g. VSD, ASD, PDA)

6. *GI tract*

- Duodenal/jejunal /biliary atresia

7. *Neuromuscular*

- Hypotonia

8. Hematopoietic
  - More chances of acute leukaemia
9. Skeletal
  - Short stature

**563. What are features of Turner's syndrome?**

**Ans.** It is X-linked disorder characterised by monosomy X (45XO) and affects the females. The features of this syndrome are:

- Short stature
- Primary amenorrhoea
- Poorly developed secondary sexual characters
- Webbing of neck
- Shield breast (flat breast)
- Cubitus valgus
- Short 4th metacarpal or metatarsal
- Coarctation of aorta
- Peripheral lymphoedema
- Nail hypoplasia.

**564. What are different body proportions in dwarfism?**

1. *The upper segment and lower segment are equal.* The causes are; hereditary, constitutional and hypopituitarism
2. *The upper segment is more than lower segment.* The causes are; achondroplasia and hypothyroidism (cretinism, juvenile hypothyroidism)
3. *Upper segment is less than lower segment.* It occurs in spinal deformities.

**565. What is cretinism? What are its features? How does it differ from pituitary dwarf?**

**Ans.** Hypothyroidism dating from birth and resulting in developmental abnormality is termed as cretinism. The characteristic features are:

- Short stature
- Dull idiotic face
- The child is lazy and lethargic
- Coarse features with protruding tongue, broad flat nose and widely-set eyes (hypertelorism), thick lips
- Sparse hair and dry skin
- Pot belly (protuberant abdomen) with an umbilical hernia

- Impaired mental development, delayed milestones development
- Retarded bone age
- Epiphyseal dysgenesis and delayed dentition
- Constipation

The difference between cretinism and pituitary dwarf are given in Table 1.145.

**Table 1.145:** Cretinism vs pituitary dwarfism

<i>Cretinism</i>	<i>Pituitary dwarfism</i>
Coarse facies, large tongue, depressed nose	Chubby juvenile facies
Low or lack of intelligence	Normal intelligence
Normal sexual development	Sexual infantilism

**566. How does hypothyroidism manifests in neonates?**

**Ans.** It manifests as

- Persistence of jaundice in neonates
- Constipation
- A hoarse cry
- Somnolence
- Feeding problem

**567. How will you proceed to investigate a patient with short stature?**

**Ans.** Various tests and conditions for which they are done are tabulated (Table 1.146).

**568. How will you treat dwarfism?**

**Ans.** Correction of primary medical disorder is the treatment of choice for growth failure. The GH or IGF-1 therapy can improve the growth of the child but complete gain of the height may not be possible without correction of underlying cause.

- *Treatment of constitutional delay of growth and adolescence (CDGA).* This condition is a normal variant in which children have short stature with normal growth rate during childhood. They have delayed puberty and attenuated pubertal growth rate. The GH is normal or low for the skeletal age but lower than normal for chronological age. The final height remains lower than predicted height in this group. These cases can be managed after careful assessment with sex steroids for few months. In girls, low dose

**Table 1.146:** Investigations for short stature

<i>Tests</i>	<i>For</i>
Complete hemogram	Anaemia (chronic infection, worm infestation)
ESR	Inflammatory bowel disease, tuberculosis
Urine pH	Renal tubular acidosis (RTA)
Ca <sup>++</sup> , PO <sub>4</sub> <sup>+++</sup> and alkaline phosphatase	Hypoparathyroidism, metabolic bone disease
Stool for ova and cysts	Intestinal infestation (hook worm, giardiasis)
Blood urea, nitrogen, SGOT and SGPT	Renal and liver disease
Radiology (X-ray skull and hands)	Bone age and pituitary fossa assessment
Thyroid function tests	Primary and secondary hypothyroidism
Chromosomal karyotyping	Gonadal dysgenesis
GH level and provocative test	GH deficiency

oestrogen may be used. The bone age acceleration does not occur with this therapy.

- *Treatment of GH failure:* GH can be used in growth hormone deficiency and even non-growth hormone deficient short statured children.

The dose of human GH (recombinant) is 0.175 to 0.35 mg/kg/week subcutaneously preferably at bed time for 6-7 weeks. The growth accelerates from 3-4 cm/yr to 10-12 cm/yr in first year. It slows down in 2nd year of therapy. Treatment is continued till target height is achieved and then dose adjusted so that

growth of child is maintained to >4 cm/yr. The side effects of the therapy is development of leukaemia and intracranial tumour.

- *Treatment of short stature due to other causes:* GH has been used with growth failure not due to GH deficiency with same success. It is indicated in children with dwarfism (>2.5 SD below the mean of age) but do not have GH deficiency. Many of these children show short-term increase in growth rate in response to GH therapy but whether their final target height will be achieved or not has not be established.

**CASE 41: TALL STATURE**

A 17-year male presented with increase in height with non-development of facial hair and small genitalia. His height is 6'-3" (Fig. 1.41A).



**Fig. 1.41A:** Tall stature. A patient with hypogonadotrophic hypogonadism—Kallmann syndrome

**569. What is your diagnosis?**

**Ans.** Tall stature due to hypogonadism, the cause of which has to be found out.

**570. What is stature?**

**Ans.** Stature means total height from crown to heel. Tall stature means height above 97th percentile of normal population of same age and sex.

**571. What is eunuchoidism?**

**Ans.** Leydig cell failure (loss of androgens or testosterone) prior to puberty results in hypogonadism, arrest of sexual maturation and tall stature due to failure of closure of the epiphyses – a condition called *eunuchoidism*, which in addition includes an infantile amount and distribution of body hair and poor muscle mass.

In common sense, androgens loss reflects eunuchoidism

**572. What do you understand by the term body proportion? What are different body proportions in tall stature?**

**Ans.** Body proportion means ratio of upper segment (vertex to pubis) to lower segment (pubis to sole) which

is 0.93 in adults because legs grow faster than trunk. The different body proportions in tall stature are:

1. The upper segment is equal to lower segment (1:1) in;
  - Gigantism
  - Kallmann syndrome
  - Frohlich's syndrome
  - Constitutional cause
2. The lower segment > upper segment is seen in;
  - Marfan's syndrome
  - Klinefelter's syndrome
  - Hypogonadism
  - Homocystinuria
4. Upper segment > lower segment
  - Precocious puberty
  - Adrenal cortical tumours

**573. What are causes of tall stature?**

**Ans.** These are:

- Constitutional
- Racial
- Marfan's syndrome
- Klinefelter's and Reifenshtein's syndromes
- Gigantism, acromegaly
- Hypogonadotrophic hypogonadism (Kallmann's syndrome, Frohlich's syndrome)
- Homocystinuria
- Congenital contractural archnoidactyly
- Super-males (XYY) and super-females (triple X)

**574. What is Kallmann's syndrome?**

**Ans.** It is a congenital disorder inherited as an X-linked recessive trait, characterised by prepubertal hypogonadotrophic hypogonadism (low testosterone, low LH and FSH levels) due to GnRH deficiency associated with eunuchoidism, small testes, scanty pubic hair (Fig. 1.41A) and anosmia (loss of smell) as a result of defect in the developing olfactory tract. In some cases, cerebellar dysfunction, cleft palate and congenital deafness are present. Cryptorchidism may occur.

**575. What is Marfan's syndrome? What are its characteristic features?**

**Ans.** Marfan's syndrome (Fig. 1.41B) is an autosomal dominant disorder characterised by two of the three (a triad) abnormalities:

1. Musculoskeletal



**Fig. 1.41B:** Marfan's syndrome. Note tall stature on measurement. Height is 6'-1½"; Arm span 6'-6" upper segment 31½"; Lower segment 42"; Ratio 0.75

2. Ocular
3. Cardiovascular

The clinical features are given in Table 1.147.

Marfan's habitus refers to presence of some of skeletal abnormalities without other features of Marfan's syndrome.

**Table 1.147:** Features of Marfan's syndrome

#### 1. Musculoskeletal

- Tall with long slender limbs
- Lower segment > upper segment
- Arachnodactyly (long slender fingers)
- Arm span > total height
- Hypotonic muscles
- Narrow face, high-arched palate and dolichocephalic skull
- Hyperextensible joints and laxity of ligaments leading to recurrent dislocation of hip and femoral and inguinal hernias
- Kyphoscoliosis, pectus carinatum or excavatum
- *Steinberg's sign or thumb protrusion sign*- in which the thumb when apposed across the palm protrudes beyond the ulnar border of the hand
- *Wrist sign* – the thumb and little finger overlap when elapsed around the opposite wrist.
- Metacarpal index > 8 (the average ratio of lengths/breadth of last 4 metacarpals from 2nd to 5th as seen on X-ray).

#### 2. Ocular

- Ectopia lentis – upward bilateral dislocation of lens, may be seen on slit lamp examination
- Myopia with blue sclera
- Squint, nystagmus
- Iridodonesis may be seen

#### 3. Cardiovascular

- Dissecting aneurysm of aorta
- Aortic regurgitation
- Conduction abnormalities.

#### 576. What is the basic defect in Marfan's syndrome?

**Ans.** Being a heritable (autosomal dominant) disorder of connective tissues the basic defect lies in gene mutation of single allele of the fibrillin gene (FBNI).

#### 577. Is eunuchoidism a feature of Marfan's?

**Ans.** No, eunuchoidism refers to androgen deficiency leading to tall stature. The patients with Marfans have normal sex characters and sexual development.

#### 578. What are causes of arachnodactyly?

- Ans.**
1. Marfan's syndrome
  2. Congenital contractural arachnodactyly.

#### 579. What are features of Klinefelter's syndrome (47 XXY Fig. 1.41C)?

**Ans.**

- Eunuchoidism (lower segment > upper segment)
- Gynaecomastia
- Hypogonadism (small firm testes)
- Phenotypically male
- Buccal smear shows barr bodies (chromosomal pattern is 47, XXY)
- Azoospermia may occur
- Gonadotropin levels are high (hypergonadotrophic hypogonadism)
- Mental subnormality (sometimes)



**Fig. 1.41C:** Klinefelter's syndrome—46 XXY (hypergonadotrophic hypogonadism). Note bilateral gynaecomastia, small testes (< 1 cm), scanty pubic hair, smaller size of penis and eunuchoidism



The triad for Klinefelter's syndrome is eunuchoidism, gynaecomastia and hypogonadism

**580. What are features of homocystinuria?**

**Ans.** Following are the features:

- It is genetic disorder inherited as autosomal recessive
- There is reduced activity of the enzyme – cystathionine beta-synthetase
- Mental retardation
- Osteoporosis is common
- Ectopia lentis with displacement of lens downward (in Marfan's, lens is displaced upwards), glaucoma and impaired visual acuity may result
- Thrombotic episodes may occur
- Plasma methionine and homocysteine are raised and cysteine is low. The cyanide-nitroprusside test is positive.

**CASE 42: GYNAECOMASTIA**

A-18-year male presented with enlargement of breasts with scanty facial, axillary and pubic hairs (Fig. 1.42).



**Fig. 1.42:** Gynaecomastia. A young adolescent male with bilateral gynaecomastia

**581. What is the clinical diagnosis?**

**Ans.** Bilateral gynaecomastia.

**582. What is gynaecomastia?**

**Ans.** The enlargement of breast in the male like that of female is called *gynaecomastia*.

**583. What are the key points to be asked or seen in a patient with gynaecomastia?**

**Ans.** Following are the key points to be noted:

- Age of the patient
- History of taking drugs, mumps or castration or prostatic cancer in old persons
- Unilateral or bilateral
- Stature of the patient and look for eunuchoidism
- Palpate the breast tissue with fingers and then with flat of the hands to confirm glandular tissue
- Examine both the testes for size, consistency
- Look for secondary sexual characters,, e.g. moustache, axillary and pubic hair
- Look for signs of chronic liver disease and hepatocellular failure

- Look for signs of superior mediastinal compression or tuberculosis or collapse of the lung
- Look for presence of leprosy

**584. What are the causes of gynaecomastia?**

**Ans.** Gynaecomastia may be physiological (newborn, adolescence and old age) or pathological resulting from imbalance between the circulating oestrogens and androgens, i.e. either oestrogen excess or androgen deficiency or insensitivity (Table 1.148).

**Table 1.148:** Causes of gynaecomastia

**I. Oestrogen excess**

- Testicular or adrenal tumours (oestrogen-secreting)
- Exogenous oestrogens (oestrogen use)
- Obesity
- Hereditary

**II. Androgen deficiency**

- *hCG producing tumour*, e.g. testes, liver,
- Endocrinopathies, e.g. hyperthyroidism, acromegaly, Cushing's syndrome, true hermaphroditism
- Miscellaneous, e.g. chronic illness, starvation/ refeeding, cirrhosis of liver, renal failure, local trauma
- *Drugs*, e.g. spironolactone, oestrogen, digitalis, cimetidine, methyldopa, isoniazid, phenothiazines, diazepam, amphetamines, cytotoxic agents

**585. How will you evaluate a case with breast enlargement in a male?**

**Ans.** Breast enlargement in a male may be due to enlargement of breast tissue (gynaecomastia) or nonbreast fatty tissue (pseudogynaecomastia). The clinical evaluation is depicted in Table 1.149.

**586. What are the causes of pseudogynaecomastia?**

**Ans.** Causes are:

- Fat deposition
- Neoplasm
- Neurofibromatosis
- Factitious

**587. How will treat a case with gynaecomastia?**

**Ans.** Treatment of gynecomastia is:

- Find out the underlying cause and treat it, i.e. treatment of leprosy, hepatocellular failure. If drug is the cause, withdraw it.

**Table 1.149:** Clinical evaluation of breast enlargement

<i>Newborn</i>	<i>Prepubertal onset</i>	<i>Pubertal onset</i>		<i>Postpubertal</i>
<ul style="list-style-type: none"> <li>Physiological bilateral gynaecomastia</li> <li>Exposure to oestrogens</li> </ul>	<ul style="list-style-type: none"> <li>Drugs</li> <li>Idiopathic</li> <li>Neoplasm (oestrogen producing)</li> </ul>	<i>Genitalia</i>		<ul style="list-style-type: none"> <li>Testicular failure</li> <li>Drug-induced</li> <li>Cirrhosis liver</li> <li>Thyrotoxicosis</li> <li>CRF</li> <li>Starvation/refeeding</li> <li>Neoplasm</li> <li>Idiopathic</li> </ul>
		<i>Normal</i>	<i>Ambiguous</i>	
		<ul style="list-style-type: none"> <li>Pubertal gynaecomastia</li> <li>Klinefelter's syndrome</li> </ul>	<ul style="list-style-type: none"> <li>Mixed gonadal dysgenesis</li> <li>Androgen resistance</li> <li>True hermaphroditism</li> </ul>	

- Pubertal gynaecomastia is painless, self-limiting, and disappears within 2 years.
- Therapy is indicated if gynaecomastia causes pain, embarrassment and emotional discomfort
- Medical therapy with testosterone is indicated in androgen deficiency. Antioestrogen therapy with

tamoxifen is indicated if oestrogen excess is the cause

- Surgery (simple mastectomy or liposuction) is indicated if medical therapy fails or gynaecomastia shows continued growth or for cosmetic and psychological reasons.

**CASE 43: HIRSUTISM**

A young 20-year female presented with excessive hair growth on face and the body like a male (beard, mustache, chest) (Fig. 1.43).



**Fig. 1.43:** Hirsutism. A young female patient with beard (growth of hairs on chin)

**588. What is the clinical diagnosis?**

**Ans.** Hirsutism

**589. What do you mean by hirsutism?**

**Ans.** Hirsutism is defined as male pattern of hair growth in women.

**590. What are the causes of hirsutism? What is virilisation and defeminisation?**

**Ans.** Androgens are responsible for differential hair distribution in women. **Virilisation** means androgen excess in women. It causes deepening of voice, temporal balding, acne, greasy skin, clitoromegaly, hirsutism and

increased muscle mass. Therefore, hirsutism is divided into two groups (i) *without virilisation*, (ii) *with virilisation* (Table 1.150). **Defeminisation** means diminishing female characters, e.g. decrease in breast size, loss of female body contours, amenorrhoea.

**591. How will you investigate such a case?**

**Ans.** Following investigations are done:

## 1. Serum androgens

Dihydroepiandrosterone (DHEAS) >8000 ng/ml and serum testosterone >2 ng/ml suggest adrenal neoplasm or congenital adrenal hyperplasia

2. Other hormones assay, e.g. TSH, ACTH, cortisol, prolactin. A short ACTH stimulation test may be performed if needed for congenital adrenal hyperplasia.
3. LH and FSH and their ratio. The LH: FSH ratio >3:1 suggest polycystic ovarian disease.
4. Glucose tolerance test (GTT) and insulin levels for polycystic ovarian disease. This would help to establish insulin resistance that occurs in polycystic ovarian disease.
5. USG of ovaries for polycystic disease (10 or more ovarian cysts > 2 mm in diameter, increased ovarian stroma and a thickened capsule suggest polycystic ovarian disease).
6. Laparoscopy and biopsy of the ovary for ovarian neoplasm
7. CT scan of adrenals for adrenal tumour.

**592. What is polycystic ovarian disease?**

**Ans.** Polycystic ovarian disease, a severe form of which is called *Stein-Leventhal syndrome* is characterised by

**Table 1.150:** Causes of hirsutism

<i>Hirsutism without virilisation</i>	<i>Hirsutism with virilisation</i>
<ul style="list-style-type: none"> <li>• Familial</li> <li>• Idiopathic</li> <li>• Polycystic ovarian syndrome (mild)</li> <li>• Late-onset congenital adrenal hyperplasia</li> <li>• Adrenal tumours</li> <li>• Cushing's syndrome, acromegaly and hyperprolactinaemia</li> <li>• Drug-induced</li> </ul>	<ul style="list-style-type: none"> <li>• Polycystic ovarian syndrome (severe)</li> <li>• Ovarian neoplasms</li> <li>• Congenital adrenal hyperplasia</li> </ul>

Note: Androgens in women are derived both from ovaries and adrenals as well as from peripheral conversion, hence, cause lies either in the ovary or adrenal

multiple ovarian cysts and excessive androgen production from the ovaries and adrenals.

The clinical features are:

- Symptoms onset immediate after menarche
- Amenorrhoea/oligomenorrhoea
- Hirsutism or acne
- Obesity
- Mild virilisation in severe cases
- Insulin resistance associated with menstrual irregularity, hypertension, hyperlipidemia
- The diagnosis is confirmed by typical ultrasonic findings and raised LH with normal or low FSH with LH: FSH ratio >3:1.

**593. What are other conditions associated with insulin resistance?**

Ans. Besides polycystic ovarian disease, the other conditions are;

- Obesity
- Lipodystrophies
- Ataxia-telangiectasia
- Werner syndrome
- Alstrom syndrome
- Pineal hyperplasia syndrome.

**594. How will you proceed to treat such a case?**

Ans. The treatment is as follows;

1. In case it is drug-induced, stop the offending drug. If it is due to a tumour, surgical removal is indicated.

2. Adrenal steroidogenic defects are treated with glucocorticoids to suppress excess ACTH and inhibit adrenal androgen secretion.
3. In idiopathic cases and in polycystic ovarian disease both cosmetic treatment (concealment or removal of hair from exposed skin areas) and suppression of androgen production or antagonism of its action by antiandrogens, e.g. cyproterone, flutamide, spironolactone, cimetidine and 5-alpha-reductase inhibitor (finasteride).

**595. Name the few drugs that produce hirsutism?**

Ans. The drugs are:

- |             |                       |
|-------------|-----------------------|
| • Phenytoin | • Oral contraceptives |
| • Androgens | • Diazoxide           |
| • Psoralens | • Minoxidil           |

**596. What is adrenal virilisation in female? What is its commonest cause?**

Ans. Adrenal androgen excess results from excessive production of dihydroepiandrosterone and androstenedione which are converted into testosterone resulting in virilisation, hirsutism, acne and oligomenorrhoea.

Congenital adrenal hyperplasia is the commonest cause of virilisation in female. It is characterised by excess of androgens with low or normal levels of glucocorticoids and mineralocorticoids.



**CASE 44: BELL'S PALSY**

A young female (Fig. 1.44) presented with asymmetry of face, difficulty in closing the eye with dribbling of saliva from one angle of the mouth on left side of face. The episode occurred following sudden exposure to cold wind in the morning. Examination revealed flattening of nasolabial fold on left side of face with inability to close the left eye. Patient could not make furrows over her forehead on the left side.



**Fig. 1.44:** Bell's palsy (idiopathic 7th cranial nerve infranuclear paralysis of left side)

**597. What is your clinical diagnosis?**

**Ans.** All the above features suggest infranuclear 7th nerve palsy probably Bell's palsy on left side.

**598. What is Bell's palsy?**

**Ans.** It is an acute infranuclear (LMN type) palsy of 7th cranial (facial) nerve involving all the muscles of face. The cause is unknown (idiopathic) though a viral aetiology is suspected. The lesion is nonsuppurative inflammation or oedema of the nerve at the level of stylomastoid foramen, hence, lacrimation and taste sensation are not reduced. Hyperacusis does not occur.

**599. What is Bell's phenomenon?**

**Ans.** An attempt to close the involved eye by the patient with Bell's palsy produces rolling of the eyeball upwards, is called *Bell's phenomenon*.

**600. What are the differences between supranuclear (UMN) and infranuclear (LMN) 7th cranial nerve palsy?**

**Ans.** Read "clinical methods in medicine" Vol. I by Dr SN Chugh.

**601. How will you localise the lesion in infranuclear 7th cranial nerve paralysis?**

**Ans.** In a lower motor neuron facial paralysis, it is important to obtain a history of diplopia, lacrimation, hyperacusis and taste sensation to localise the level of the lesion (Table 1.151).

**602. What are the causes of facial nerve palsy?**

**Ans.** The facial paralysis may be supranuclear (UMN type), nuclear and infranuclear (LMN type). The causes are enlisted in Table 1.152.

**603. What is Ramsay Hunt syndrome?**

**Ans.** It is herpetic infection of geniculate ganglion. It is characterised by:

**Table 1.151:** Localisation of lesion in facial nerve paralysis.

Site of lesion	Features
A. Stylomastoid foramen (Bell's palsy)	A. Paralysis of all muscles of facial expression only.
B. Facial canal (chorda tympani branch is involved)	B. Features described above (A) <i>plus</i> loss of taste sensation from anterior two-thirds of tongue
C. A higher lesion in facial canal (nerve to stapedius is damaged)	C. Features described above in A <i>plus</i> hyperacusis
D. Geniculate ganglion	D. In addition to features of A, there is loss of lacrimation and salivation. 8th nerve may also be involved
E. In pons	E. 6th and 7th cranial nerve palsy (Millard–Gubler syndrome)
F. Cerebellopontine angle	F. The facial nerve, 8th cranial nerve and nervus intermedius involved

**Table 1.152:** Causes of facial nerve paralysis

<b>A. Unilateral palsy</b>	<b>B. Bilateral palsy</b>
<b>I. Supranuclear paralysis</b>	<b>I. Supranuclear</b>
<ul style="list-style-type: none"> <li>• CVA</li> <li>• Neoplasm</li> <li>• Demyelinating diseases, e.g. multiple sclerosis</li> </ul>	<ul style="list-style-type: none"> <li>• Cerebral atherosclerosis</li> <li>• Double hemiplegia</li> <li>• Pseudobulbar palsy</li> </ul>
<b>II. Nuclear paralysis</b>	<b>II. Infranuclear and nuclear</b>
<ul style="list-style-type: none"> <li>• Brainstem infarction and neoplasm</li> <li>• Poliomyelitis</li> </ul>	<ul style="list-style-type: none"> <li>• Acute Guillain-Barre syndrome</li> <li>• Leprosy</li> <li>• Sarcoidosis</li> <li>• Leukaemia or lymphoma</li> <li>• Forceps delivery</li> <li>• Bilateral Bell's palsy</li> <li>• Bilateral otitis media</li> <li>• Myasthenia gravis</li> </ul>
<b>III. Infranuclear paralysis</b>	
a. <i>Intracranial involvement</i>	
<ul style="list-style-type: none"> <li>• Cerebellopontine angle tumour (e.g. acoustic neuroma, meningioma)</li> <li>• Meningitis</li> <li>• Meningovascular syphilis</li> <li>• Fracture of temporal bone</li> <li>• Otitis media</li> <li>• Herpes zoster infection of geniculate ganglion (Ramsay Hunt Syndrome)</li> <li>• Glomus jugulare tumour</li> </ul>	
b. <i>Extracranial involvement</i>	
<ul style="list-style-type: none"> <li>• Hansen's disease (leprosy)</li> <li>• Mixed parotid tumours</li> <li>• Sarcoidosis</li> <li>• Bell's palsy (it is the commonest)</li> </ul>	

- Fever with headache, bodyache
- Herpetic vesicles/rash on the tympanic membrane, external auditory meatus and pinna.
- Loss of taste in anterior two-thirds of the tongue
- Hyperacusis on the affected side
- LMN type of ipsilateral facial nerve palsy.

**604. How will you diagnose bilateral UMN type of 7th nerve paralysis?**

**Ans.** In bilateral supranuclear palsy, the upper part of face is not spared (i.e. total face is paralysed), hence, there will be:

- Mask like face
- Emotion preserved
- Exaggerated jaw jerk
- Absence of Bell's phenomenon
- Glabellar tap is positive
- Double hemiplegia (long tracts signs on both the sides).

**605. What are the complications of Bell's palsy?**

**Ans.** Following are the complications:

- Exposure keratitis and corneal ulceration

- Hemifacial spasms
- Crocodile tears
- Social stigma

**606. What are crocodile tears?**

**Ans.** Watering of the eye (lacrimation) on the paralysed side during chewing is called "*Crocodile tears*". These are due to aberrant re-innervation of the lacrimal gland by fibres originally meant for the salivary gland.

**607. What is hemifacial spasm?**

**Ans.** Hemifacial spasm is characterised by the narrowing of the palpebral fissure on the affected side and pulling of the angle of the mouth due to contraction of facial muscles. The spasms may be *post-paralytic* or "*essential*". The pathogenesis is compression of the facial nerve by loops of cerebellar arteries or by AVM (arterio-venous malformation), or aneurysm or a cerebello-pontine angle tumour.

**608. How will you manage a case with Bell's palsy?**

**Ans.** Management of Bell's palsy includes:

1. NSAIDs for inflammation and relief of pain.

2. A short course of steroids (40-60 mg of prednisolone for few days then tapered over next 2-3 weeks) is given to reduce oedema around the nerve.
3. Galvanic current stimulation of the paralysed muscles may help.
4. If no improvement occurs within 6 weeks, the surgical decompression at the stylomastoid foramen is advised.
5. Facial exercises in front of a mirror are advised.

**609. What is mimic facial nerve palsy?**

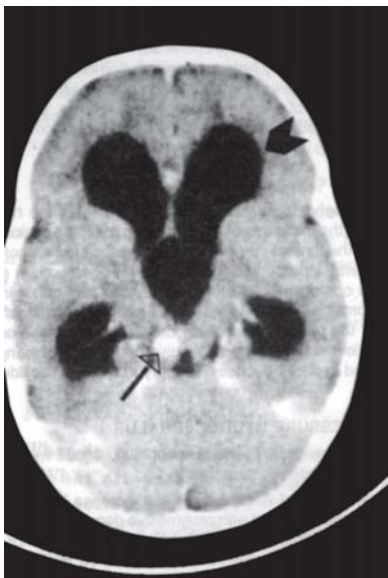
**Ans.** Mimic palsy refers to preservation of voluntary movements but the emotional movements of the facial muscles are lost. This is seen in frontal lobe lesion. It is due to the fact that UMN fibres for emotion have a different course than the pyramidal tract.

### CASE 45: HYDROCEPHALUS AND RAISED INTRACRANIAL PRESSURE

A 35 years male presented with headache, generalised in nature occurring commonly during morning hours on getting up. There was history of projectile vomiting and blurring of vision. There was history of convulsions but no focal neurological deficit. Examination revealed bilateral 6th nerve palsy and papilloedema. There was no disturbance in consciousness. All the reflexes were exaggerated. Sensory system was normal. No neck stiffness was detected (Figs 1.45A and B).



**Fig. 1.45A:** Patient with raised intracranial pressure



**Fig.1.45B:** CT scan showing dilated ventricular system. The (↑) arrow indicate the causative lesion

#### 610. What is your probable diagnosis?

**Ans.** The persistent morning headache with projectile vomiting and papilloedema in a young male with no localising sign and no net neurological deficit suggest the diagnosis of raised intracranial tension the cause of which has to be found out.

#### 611. What is benign raised intracranial tension?

**Ans.** The term benign or idiopathic raised intracranial pressure is used to signify increased intracranial pressure (ICP) produced by diffuse swelling of brain and characterised by a triad of symptoms (headache, vomiting, papilloedema) and dilated ventricular system. The CSF pressure is raised but CSF analysis is normal. Neuroimaging is normal except dilated ventricles. The other terms used for this condition are:

- Otitic hydrocephalus
- Pseudotumour cerebri
- Serous meningitis

Benign intracranial hypertension is diagnosed by exclusion of all other causes that produce raised ICP.

#### 612. What are the causes of benign intracranial hypertension (BIH)?

**Ans.** A variety of conditions are known to produce BIH such as:

- Hypervitaminosis A
- Hypoparathyroidism
- Prolonged steroid therapy
- Addison's disease
- Severe anaemia
- Pregnancy
- Middle-aged female with obesity
- Drug-induced, e.g. tetracyclines, ampicillin, amphotericin B and ciprofloxacin.

#### 613. What are the conditions that come into differential diagnosis of BIH?

**Ans.** Two important conditions that result in identical clinical picture are;

- Neurocysticercosis
- Cortical venous sinus thrombosis

#### 614. What is hydrocephalus?

**Ans.** The term *hydrocephalus* (*hydro* means excess of water, *cephalus* means head) implies dilatation of the

**Table 1.153:** Causes of raised intracranial pressure (ICP) or hydrocephalus

<b>I. Congenital obstruction</b>
• Arnold-Chiari malformation
• Aqueductal stenosis
• Dandy-Walker syndrome
• Agenesis of arachnoid villi
<b>II. Trauma to head (head injuries)</b>
<b>III. Infections</b>
• Bacterial meningitis (tubercular, pyogenic)
• Encephalitis
• Cerebellar abscess
<b>IV. Intracranial bleed</b>
• Cerebral haemorrhage
• Subarachnoid haemorrhage
• Hypertensive encephalopathy
<b>V. Space occupying lesions</b>
• Brain tumours, e.g. craniopharyngioma, medulloblastoma, astrocytoma, ependymoma, metastases
<b>VI. Venous obstruction</b>
• Cortical thrombophlebitis
• Dural sinus thrombosis
<b>VII. Benign (idiopathic)</b>
Read the causes of BIH as already discussed

ventricles of brain due to excessive accumulation of CSF. It may be associated with raised, normal or low ICP. Raised ICP with hydrocephalus is called *hypertensive hydrocephalus*.

### 615. What are the causes of raised intracranial tension or hydrocephalus?

**Ans.** All the cases of hydrocephalus have increased intracranial pressure except normal pressure hydrocephalus. Raised ICP results either due to excessive production of CSF or obstruction to circulation or impaired absorption of cerebrospinal fluid in the brain. The causes of hydrocephalus and increased intracranial pressure are more or less same (Table 1.153).

### 616. What are false localising signs?

**Ans.** There are certain signs which do not have localising value, often bilateral but can be unilateral, occur in ICP called *false localising signs*. These are:

- Bilateral or unilateral 6th nerve palsy
- Bilateral or unilateral 3rd nerve palsy (pupillary changes)
- Bilateral plantar extensor responses
- Bilateral mild cerebellar dysfunction
- Mild endocrinal dysfunction.

### 617. What do you understand by herniation of brain? What are various types of herniation syndromes seen in raised ICP?

**Ans.** The rise in ICP is equally distributed throughout the cranial cavity between supratentorial and infratentorial compartments through the tentorial opening containing the brainstem. When the tentorial opening is blocked, then there is differential distribution of ICP between the two compartments resulting in herniation (protrusion of a part of brain) syndromes.

The types of herniation are:

- Supratentorial (uncus herniation):** There is herniation of uncus of medial temporal lobe resulting in;
  - Contralateral hemiparesis due to compression and displacement of ipsilateral crus cerebri- *Kernohan Woltman Sign*
  - Ipsilateral hemiparesis due to compression of contralateral crus against the tentorium – a *Kernohan's notch*. It is due to contracoup effect seen in a mass lesion
  - Pupillary dilatation and paresis of extraocular muscles due to stretching of ipsilateral 3rd nerve.
- Infratentorial (cerebellar tonsillar herniation).** Increased ICP in infratentorial compartment results in tonsillar coning compressing the medulla oblongata resulting in respiratory irregularities or distress and cardiovascular arrest.
- Transtentorial central herniation** in which brainstem protrudes through the tentorium resulting in;
  - Occipital headache, neck rigidity
  - Decorticate posturing
  - Bradycardia and hypertension
  - Bilateral plantar extensor responses
  - Dilated and fixed pupils
  - Brain death.

### 618. What is normal ICP?

**Ans.** Normal intracranial pressure within cranial cavity measured indirectly is 5-10 mmHg. Any ICP above 15 mmHg is taken as raised intracranial pressure.

Now-a-days ICP can be measured directly by devices implanted in the lateral ventricle or intraparenchymal placement.



**619. How will you investigate such a case?**

**Ans.** Following investigations are done:

1. **X-ray skull:** It may reveal sutural diastasis (separation of sutures) in infants, thinning and increased convolutional markings (*Silver-beaten appearance*) in adolescents and adults.  
In addition, the brunt of changes are seen in sellar region, e.g. destruction of anterior clinoid processes, enlargement of sella turcica.
2. **CT scan:** reveals dilatation of ventricular system, cortical thinning, effacement of cisterns, an underlying lesion and periventricular lucency and compression of ventricle (s)
3. **MRI:** It can differentiate between vasogenic and cytopathic cerebral oedema seen in patients with ICP and predicts response to shunts.
4. **Measurement of ICP:** It confirms the diagnosis. Ventriculography and pneumoencephalography are not performed now-a-days.

**620. What is normal pressure hydrocephalus, occult hydrocephalus?**

**Ans.** A syndrome of dilated ventricles with normal intracranial pressure associated with a triad of symptoms, i.e. dementia, ataxia and urinary incontinence in older persons is called normal *pressure hydrocephalus*. This is actually a misnomer. It is a communicating hydrocephalus in which CSF hemodynamics compromise and result in normal pressure. Though, it may be seen in patients with head injury, hypertensive haemorrhage or meningitis but in majority of cases no cause is identified.

**621. How will you diagnose hydrocephalus in a child?**

**Ans.** The diagnosis is based on:

1. Abnormal enlargement of head. An increase in head circumference by  $>1$  cm in every 2 weeks

on serial measurements for the first three months of life makes the paediatrician suspicious.

2. Separation of sutures of skull
3. Bulging of anterior fontanelle
4. "Setting-sun sign"- the eyeballs appear to be pushed down and upper bulbar conjunctivae become visible
5. Scalp veins are dilated
6. High-pitched cry
7. The skull is resonant, gives "cracked pot sound" on percussion (*Macewen's sign*).

**622. What is treatment of raised ICP or hydrocephalus?**

**Ans.** Following treatments are advocated:

1. **The drug therapy to reduce the ICP include;**
  - Mannitol (20%), e.g. 100 ml IV 4-6 hourly
  - Glycerol (10%), e.g. 1.2 g/kg over 4 hours
  - Dexamethasone (10-20 mg/day in divided doses)
  - Frusemide, e.g. 20-40 mg IV
  - Acetazolamide (50-75 mg/kg/day)
2. **Shunt surgery**
  - The various shunts performed are;
  - Ventriculoperitoneal shunt (commonly used)
  - Endoscopic third ventriculostomy
  - Endoscopic placement of a stent in cerebral aqueduct in aqueductal stenosis.
3. **Repeated lumbar puncture** in a patient with benign raised intracranial pressure may be helpful to reduce ICP.

**CASE 46: PARKINSONISM**

A 60-year-male presented with history of slowness of movements, difficulty in writing, disturbance in speech and slowness during activity and walking. Examination revealed mask-like face, slowness of various motor acts, tremors at rest, soft monotonous stuttering speech and abnormal (short-shuffling) gait. There was increased tone (rigidity), stooped posture and reflexes were normal (Fig. 1.46).



**Fig. 1.46:** Parkinsonism. There is stooped posture with short-shuffling gait

**623. What is the probable clinical diagnosis and why?**

**Ans.** A combination of slowness of activity (bradykinesia), rigidity and tremors at rest with disturbance of speech and gait suggest the diagnosis of Parkinsonism.

**624. What is parkinsonism? What is parkinsonian plus syndrome?**

**Ans.** Parkinsonism is a movement disorder due to involvement of extrapyramidal system (basal ganglia) and is characterised by tremors, rigidity, akinesia or bradykinesia and postural disturbances. This is also called *akinetic* (loss or paucity of movements) *rigid* (rigidity) syndrome.

*Parkinsonism plus syndrome* refers to parkinsonism plus bulbar palsy (progressive supranuclear palsy), multiple system atrophies, e.g. olivopontocerebellar

**Table 1.154:** Common clinical features of parkinsonism

**I. General**

- Mask-like (expressionless) face
- Stooped posture/flexed posture
- Slurred speech
- Widened palpebral fissure and infrequent blinking
- Blepharospasm
- Drooling of saliva from the mouth

**II. Bradykinesia or akinesia**

- Slowness or difficulty in initiating voluntary acts such as walking, rising from an easy chair or bed
- Impaired fine movements
- Poor precision of repetitive movements

**III. Disturbance of gait**

- Short-shuffling (festinating) gait with difficulty in stopping
- Reduced swinging of arms during walking
- Propulsion and retropulsion
- Loss of balance on turning

**IV. Tremors**

- Resting tremors, suppressed by voluntary action, disappear during sleep and aggravated by fatigue and excitement
- Limited to distal parts, e.g. pill-rolling tremors of hands, or may begin with rhythmic flexion/extension of hands with pronation and supination of the forearms.
- Sometimes, there may be fast- action tremors

**V. Rigidity**

- Cog-wheel (more in upper limbs)
- Lead pipe (more in lower limbs)

**VI. Miscellaneous**

- Positive glabellar tap (Myerson's sign). Repetitive tapping over the glabella produces a sustained blink response with each tap in contrast to the normal response where blinking becomes infrequent after few taps.
- Micrographia (small hand-writing)
- Emotional lability
- Normal tendon reflexes
- Plantars are flexors

degeneration and primary autonomic failure (*Shy-Drager syndrome*).

**625. What are clinical features of Parkinsonism?**

**Ans.** They are described in Table 1.154.

**626. What are the causes of Parkinsonism?**

**Ans.** The causes are:

1. Idiopathic Parkinson's disease
2. Secondary parkinsonism due to;
  - *Viral infection*, e.g. encephalitis lethargica, Japanese B encephalitis, Creutzfeldt-Jacob disease, subacute sclerosing panencephalitis

- *Toxins*, e.g. manganese, MPTP (1-methyl 4-phenyl tetrahydropyridine), Carbon disulphide
- *Hypoxia*, e.g. cyanide, carbon monoxide
- *Vascular*, e.g. atherosclerotic
- *Metabolic*, e.g. Wilson's disease, hypoparathyroidism
- *Head injury*, e.g. Punch-drunk syndrome
- *Brain tumours*.

### 627. What is festinating gait of Parkinsonism?

**Ans.** It comprises of:

- Slow movements
- Narrow-based gait
- Short shuffling steps taken rapidly as if patient is chasing his/her centre of gravity
- Stooped posture with head-tilting forwards
- Sometimes, the feet may appear to be glued to the floor, so called *freezing phenomenon*
- The fall is characteristic like a telegraph pole. There is tendency to frequent forward falls due to postural instability.
- There is propulsion (push test) and retropulsion (pull test). The patient starts walking forward and backward when pushed or pulled.
- Due to postural instability, patient can not stop himself/herself when pushed or pulled
- There is infrequent swinging of the arms during walking.

### 628. What is glabellar sign (Refer to Table 1.154)?

**Ans.** Read Clinical Methods Vol. I by Prof S.N. Chugh.

### 629. What autonomic disturbances occur in Parkinsonism?

**Ans.** The common features of autonomic disturbance in parkinsonism are:

- Constipation
- Frequency of micturition
- Nocturia
- Excessive salivation and drooling of saliva from the mouth
- Orthostatic hypotension
- Feeling of cold
- Postural oedema
- Impotence

Autonomic disturbances are common and early in shy-Dragger syndrome (Parkinsonism plus syndrome).

### 630. What are changes in higher mental functions in Parkinsonism?

**Ans.** Following changes can be observed:

- Emotional lability (e.g. spontaneous laughter is common in manganese poisoning)
- Depression-mask like face, mood disturbance
- Anxiety
- Frontal lobe dysfunction
- Dementia is uncommon

### 631. What are the drugs available for treatment of parkinsonism?

**Ans.** The anti-parkinsonian drugs are;

#### 1. Levodopa preparations

##### 1. Levodopa (1500-6000 mg/day)

The various combinations of L-dopa are;

- Carbidopa/levodopa (25/100, 10/100, 25/250). Dose is 300-1000 mg of L-dopa /day
- Benserazide/levodopa (25/100 12.5/50) dose is 600-800 mg of L-dopa/day
- Controlled release carbidopa/levodopa (50/200). Dose is 200-800 mg/day

##### 2. Amantidine (100-200 mg/day)

##### 3. Anticholinergics

- Trihexyphenidyl (4-8 mg/day)
- Benztropine (1-1.5 mg/day)

##### 4. Antihistaminics

- Diphenhydramine (50-100 mg/day)
- Orphenadrine (150-200 mg/day)

##### 5. Dopamine agonists

- Bromocriptine (5-10 mg/day)
- Pergolide (0.1-0.2 mg/day)

##### 6. MAO-B inhibitor

- Selegiline (5-10 mg/day)

### 632. What is golden rule for the use of antiparkinsonian drugs?

**Ans.** "Start low and go slow".

### 633. What is type of speech in Parkinsonism?

**Ans.** The voice becomes soft (hypophonic), monotonous and stuttering. The speech is rapid than normal. In advanced cases, speech is reduced to muttering. Dribbling of saliva is common.

**634. What is Shy-Drager syndrome?**

**Ans.** It is called *Parkinsonism plus syndrome* and includes:

- Parkinsonism. Rest tremors are early followed by gait and postural abnormality
- Autonomic disturbance (dysautonomia), e.g. orthostatic hypotension, sphincter disturbance and impotence
- In addition, patients may have laryngeal stridor and pyramidal features.

**635. What are the causes of slowness of movements?**

**Ans.** Causes are:

- Parkinsonism
- Hypothyroidism
- Depression

**636. What is Wilson's disease?**

**Ans.** This is rare and treatable inherited (autosomal recessive) disorder of copper metabolism in which copper

is deposited in the basal ganglia (choreoathetosis), around the cornea (Kayser-Fleischer rings) and in the liver (cirrhosis) due to low levels of ceruloplasmin (copper binding protein). It occurs in young patients, therefore, young patients with cirrhosis must be screened for this condition.

The diagnosis if suspected is confirmed by;

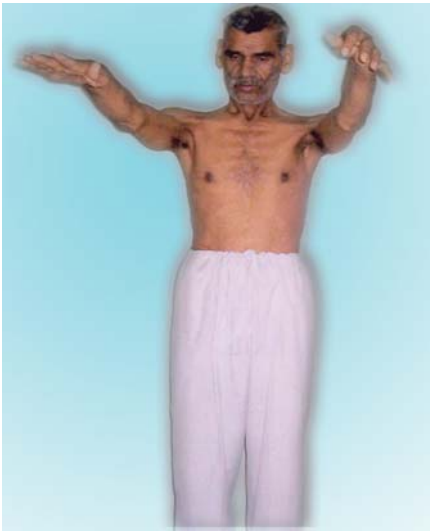
1. A serum ceruloplasmin level <200 mg/L and Kayser-Fleischer rings  
OR
2. A serum ceruloplasmin level <200 mg/L and a concentration of copper in liver biopsy >200 µg/g dry weight.

*Note:* Read the clinical methods for answers to the following questions.

1. What is tremor?
2. What is difference between fine and coarse tremors?
3. What are the causes of tremors at rest?
4. What is benign essential tremor?

**CASE 47: CHOREA**

A 36-years-male presented with wide flinging abnormal movements of upper limbs at rest. They were brief, and initiated by sudden voluntary act. They subsided during sleep. Patient had mental retardation (IQ 50-50%), and positive family history. Examination revealed no evidence of heart disease or arthritis or subcutaneous nodule or erythema marginatum. Neurological examination revealed wide-flinging, quasi-purposive involuntary movements and hypotonia. Jerks were normal. Plantars were flexor (Fig. 1.47).



**Fig. 1.47:** Chorea

**637. What is your probable diagnosis and why?**

**Ans.** Wide-flinging dancing movements of upper limbs at rest with no other finding in CVS and neurological examination suggest the diagnosis of chorea but presence of mental retardation and positive family history for the disease go in favour of Huntington's chorea.

**638. What is chorea?**

**Ans.** Choreiform movements are rapid, brief, jerky or wide-flinging, nonrepetitive and quasipurposive movements limited to face, limbs and tongue.

These movements are completely irregular and variable in time, rhythm, character and place of origin.

Chorea literally means a dance, hence movements called *dancing movements*

**639. What are the causes of chorea?**

**Ans.** The causes are:

1. *Hereditary*
  - Huntington's chorea
  - Benign hereditary chorea
  - Ataxia telangiectasia
  - Wilson's disease
2. *Infectious*
  - Sydenham's (rheumatic ) chorea
  - Postencephalitic chorea
3. *Metabolic*
  - Thyrotoxicosis
  - Hypoparathyroidism
  - Pregnancy (chorea gravidarum)
4. *Immunological*
  - SLE
  - Henoch-Schönlein purpura
5. *Drug and toxins*
  - Oral contraceptive, lithium, L-dopa, phenothiazines
  - Alcohol
  - Carbon monoxide, hypoxia, manganese
6. *Miscellaneous*
  - CVA (Hemiplegic/chorea)
  - Senile
  - Tumour (e.g. paraneoplastic)
  - Trauma
  - Hypernatraemia

**640. What are cardinal features of chorea?**

**Ans.** Cardinal features are:

1. *Pronator sign:* Ask the patient to raise both upper limbs above the head, the hands will get pronated if chorea is present.
2. *Waxing and waning of the grip- called "milking" grip or milking sign.* It is noticed when patient is asked to squeeze the examiner's hands or fingers tightly.
3. *Dinner-fork deformity:* This refers to position of the fingers when patient is asked to stretch out the hands and spread the fingers. There is hyperextension of elbows, hyperpronation of forearms, flexion of wrists with hyperextended fingers (metacarpophalangeal joints are extended with separation of fingers). It is due to hypotonia.



Table 1.155: Chorea vs athetosis

Features	Chorea	Athetosis
1. Site of lesion	Caudate nucleus	Putamen
2. Prevalence	Common	Uncommon
3. Tone	Decreased	Increased
4. Movements	Rapid, continuous, uninterrupted and quasipurposive	Slow and sinuous writhing movements, i.e. extension and supination of the arm with alternating flexion and extension of fingers
5. Effect of excitement	Increased	No effect
6. Parts involved	Proximal more than distal	Distal parts involved more than proximal
7. Tongue	Lizard tongue	Chewing tongue
8. Deep tendon jerks	Pendular or hung-up	Normal

4. *Hypotonia and instability.* It is elicited by

- *Pendular knee jerk* or hung-up reflex (a choreic movement is superimposed on a tendon jerk)
- *Lizard or reptile tongue.* When patient is asked to protrude the tongue; he/she does it and takes it back with reptile speed. The tongue when projected looks like a bag of worms.

#### 641. How will you diagnose chorea?

**Ans.** The diagnosis of chorea is clinical. Perform all the signs described above.

The simplest way to diagnose chorea is to ask the patient to raise the arms above the head with hands facing each other (Fig. 1.47). If chorea is present, the patient will tend to pronate the arms and rapid jerky movements of upper limbs will appear.

#### 642. What is the site of lesion in chorea?

**Ans.** Caudate nucleus.

#### 643. What is hemichorea?

**Ans.** Choreic movements limited to one half of the body is called *hemichorea*. Usually chorea is generalised and bilateral.

#### 644. What is “pure chorea”?

**Ans.** Pure chorea means isolated rheumatic chorea when other rheumatic manifestations (Jones major criteria) are not seen. This is due to the fact that chorea is a delayed manifestation of rheumatic fever when carditis and arthritis and other rheumatic features either have not appeared or have disappeared.

#### 645. What are the differences between Sydenham’s chorea and Huntington’s chorea?

**Ans.** Read Clinical Methods in Medicine vol. I by Dr. S.N.Chugh.

#### 646. What are various involuntary movements?

**Ans.** Read clinical methods in medicine vol. I.

#### 647. What is athetosis? How will you differentiate it from chorea?

**Ans.** Athetosis means instability of posture. It is defined as slow sinuous writhing involuntary movements involving the wrist, fingers and ankle (peripheral parts of a limb). The lesion is in the putamen. Its differentiation from chorea is given in Table 1.155.

#### 648. What is chorea gravidarum?

**Ans.** It is actually rheumatic chorea manifesting during pregnancy or postpartum period.

#### 649. What are conditions that produce irregular, rapid jerky movements of limbs?

**Ans.** These are;

- |  |   |
|--|---|
| 1. Tics. They are controlled by voluntary effort |   |
| 2. Chorea  |   |
| 3. Hemiballismus                                 | They are not suppressed by voluntary effort |
| 4. Myoclonus                                     |   |

#### 650. What is myoclonus? What are its common causes?

**Ans.** Myoclonus is rapid, irregular jerky movements of a limb due to contraction of a single muscle or a group of muscles. They occur spontaneously at rest, in response to sensory stimuli or voluntary movements.

The common causes are:

- Cerebral hypoxia (posthypoxic intention myoclonus)
- Lipid-storage disease
- Encephalitis or Creutzfeldt-Jacob disease
- Metabolic encephalopathies, e.g. liver cell failure, renal failure, respiratory failure, electrolyte imbalance, etc.
- A feature of myoclonic epilepsy.

**CASE 48. CEREBELLAR ATAXIA**

A young patient presented with unsteadiness of gait and tendency to fall on either side of the body of few months duration. The ataxia was progressive and associated with speech disturbance. Examination revealed dysarthria, nystagmus, lower limbs weakness, loss of lower limb reflexes and plantars were extensors. There was loss of joint and position sense in the lower limbs. Scoliosis and pes cavus were present. Romberg's sign was negative (Fig. 1.48).



**Fig. 1.48:** Cerebellar ataxia. Note the unsteadiness during standing (patient is being supported on both the sides)

**651. What is probable diagnosis? Give reasons in favour of your diagnosis?**

**Ans.** Progressive ataxia in a young person with dysarthria, nystagmus, loss of lower limbs reflexes and sense of position and vibration with plantars extensor indicate cerebellar ataxia, probably Friedreich's ataxia. Negative Romberg's sign supports the diagnosis and differentiates it from sensory ataxia.

**652. What is Friedreich's ataxia?**

**Ans.** It is heredofamilial ataxia (autosomal recessive) characterised by progressive degeneration of dorsal root ganglia, spinocerebellar tracts, corticospinal tracts and Purkinje cells of cerebellum.

**653. What are various cerebellar signs?**

**Ans.** As the cerebellum maintains, tone, posture, coordination and integrates the voluntary and automatic movements, hence, the tests performed are based on

these functions. A unilateral cerebellar lesion will produce these signs on the same side (ipsilateral).

1. *Hypotonia*: There is hypotonia on the side involved. The limbs are flaccid both at rest and on passive movements.
2. *Titubation*: Nodding of head may be present.
3. *Signs of incoordination in upper limbs*: Following signs indicating incoordination in the upper limbs will appear;

- *Intention tremors*: The tremors appear as the patient approaches his/her target/goal. For example, ask the patient to touch his/her nose with index finger, the tremors appear as nose is approached.
  - *Finger nose test*: This is a useful test, and positive on the side involved.
  - *Finger to finger test*- In cerebellar disease, there will be past-pointing (past-pointing is positive)
  - Dysmetria
  - Dyssynergia
  - Dysdiadochokinesia
  - Rebound phenomenon
- Read all these signs in Clinical Methods in Medicine by Prof.S.N. Chugh

4. *Signs of incoordination in lower limbs*

- Knee-heel test (positive on the side involved)
- Tandem walking (heel-to-toe walking). Patient sways on the side involved
- *Romberg's sign*. Patient sways to the side involved when he/she stands with eyes open with feet together
- *Abnormal gait* Patient sways or tends to fall to the side involved while walking

5. *Nystagmus* with fast component to the side of lesion

6. *Speech*, e.g. dysarthria (Staccato or scanning speech).

All these signs/tests have already been described and discussed in "Clinical Methods in Medicine" by Prof. S.N. Chugh.

**654. What are the causes of cerebellar ataxia?**

**Ans.** The cerebellar ataxia may be with bilateral symmetrical signs or with unilateral signs. It can be acute, subacute or chronic. The causes are given in Table 1.156.

**655. What are diagnostic criteria for Friedreich's ataxia?**

**Ans.** The diagnostic criteria (modified from Harding) are depicted in Table 1.157.

**Table 1.156:** Causes of cerebellar ataxia

<b>I. With bilateral signs</b>	
<i>Acute and subacute (&lt;6 weeks)</i>	<i>Chronic (&gt; 6 months)</i>
<ul style="list-style-type: none"> <li>• Acute cerebellitis, e.g. viral, bacterial (enteric)</li> <li>• Post – infectious syndrome</li> <li>• Toxins and drugs, e.g. alcohol, lithium, hydantoin, barbiturates</li> <li>• Lyme disease</li> <li>• Nutritional (B<sub>1</sub>, B<sub>12</sub> deficiency)</li> </ul>	<ul style="list-style-type: none"> <li>• Hereditary ataxias, e.g. autosomal dominant (spinocerebellar) and autosomal recessive Friedreich's ataxia</li> <li>• Paraneoplastic syndrome</li> <li>• Hypothyroidism</li> <li>• Tabes dorsalis</li> </ul>
<b>II. With unilateral signs</b>	
<i>Acute</i>	<i>Chronic</i>
<ul style="list-style-type: none"> <li>• Vascular, e.g. cerebellar hemorrhage, infarction or subdural hematoma</li> <li>• Infection, e.g. cerebellar abscess</li> <li>• Neoplasm, e.g. glioma and metastatic tumour</li> <li>• Demyelinating, e.g. multiple sclerosis, AIDS related multifocal leucoencephalopathy</li> </ul>	<ul style="list-style-type: none"> <li>• Congenital, e.g. Dandy- Walker syndrome, Arnold-Chiari malformation</li> <li>• Secondary gliosis in a vascular lesion</li> <li>• Old demyelinating plaques detected on MRI/CT</li> </ul>

**656. What are the causes of absent ankle jerk with extensor plantars response?**

**Ans.** Following are the causes:

- Friedreich's ataxia
- Tabes dorsalis
- Nutritional deficiency of B<sub>1</sub> and B<sub>12</sub> with ataxia
- Paraneoplastic syndrome

**657. What are the features of central (vermis) cerebellar lesion?**

**Ans.** Following are the features:

- Head nodding (titubation)
- Truncal ataxia
- Positive heel-to-toe gait (tandem gait)
- Difficulty in sitting, rising from a chair, standing and walking. There is unsteadiness and swaying during these activities

**658. What is the type of tremors in cerebellar disease?**

**Ans.** Intention tremors. An intention tremor is an involuntary movement (e.g. tremor) which becomes prominent during voluntary movement towards a target. It is absent at rest. It is demonstrated by asking the patient to touch the tip of his/her nose, tremors in the fingers appear as nose is approached.

**Table 1.157:** Diagnostic criteria for Friedreich's ataxia (FA)

<b>I. Essential criteria</b>	
<ul style="list-style-type: none"> <li>• Progressive ataxia</li> <li>• Young age (&lt;25 years)</li> <li>• Extensor plantar responses</li> <li>• Absent ankle and knee jerks</li> <li>• Dysarthria (after 5 years of onset of symptoms)</li> <li>• Motor nerve conduction velocity &gt;40 m/sec in upper limbs with small or absent sensory action potential</li> </ul>	
<b>II. Additional criteria (present in 2/3 rd patients)</b>	
<ul style="list-style-type: none"> <li>• Pyramidal weakness in lower limbs</li> <li>• Distal loss of joint position and vibration sense in lower limbs</li> <li>• Scoliosis</li> <li>• Abnormal ECG (wide spread T wave inversion and ventricular hypertrophy)</li> </ul>	
<b>III. Other supportive features (present in &lt;50% patients)</b>	
<ul style="list-style-type: none"> <li>• Nystagmus, optic atrophy</li> <li>• Pes cavus</li> <li>• Distal weakness and wasting</li> <li>• Diabetes</li> <li>• Deafness</li> </ul>	

**659. What are various types of ataxias?**

**Ans.** Ataxia is a movement disorder. A movement needs coordination of cortex, cerebellum, the reflex arc and impulses from the eyes, ears (labyrinth) and cervical spine. Hence, ataxia is of following types:

1. Cerebellar (read the causes)

**Table 1.158:** Distinction between sensory and cerebellar ataxia

Features	Sensory ataxia	Cerebellar ataxia
Muscle power	Diminished	Normal
Deep tendon reflexes	Lost	Pendular or hung-up
Cerebellar signs	Absent	Present
Posterior column sensations	Lost	Preserved
Plantar reflex	Lost	Extensor response or normal
Charcoat joint and trophic changes	Present	Absent
Romberg's sign	Positive	Negative
Gait	High-steppage or stamping gait	Broad - based gait
Common causes	Tabes dorsalis and peripheral neuropathy	Friedreich's ataxia, multiple sclerosis

2. Sensory (e.g. peripheral neuropathy, subacute combined degeneration, tabes dorsalis)
3. Labyrinthine or vertiginous ataxia, e.g. labyrinthitis, Meniere's disease, streptomycin - induced
4. *Central* (lesion lies in the medulla)
5. Miscellaneous, e.g. ataxia due to severe muscular weakness and hypotonia.

**660. What is sensory ataxia? What are its causes? What is Romberg's sign? How will you differentiate it from cerebellar ataxia?**

**Ans.** Sensory ataxia results from defective proprioceptive sensations (posterior column involvement), hence, does not occur with eyes open, as sense of position is compensated by open eyes. Thus, sensory ataxia manifests or gets increased when the eyes are closed.

**Causes**

Sense of proprioception is affected by lesions of peripheral nerves, sensory root, posterior column and post-central gyrus in parietal lobe, hence causes are:

1. Lesion of peripheral nerves, e.g. neuropathy due to any cause
2. Sensory root lesion, e.g. tabes dorsalis, radiculopathy (disc prolapse)
3. Posterior column involvement, e.g. multiple sclerosis, syringomyelia and intramedullary compression
4. *Parietal lobe lesion* (sensory cortex involvement), e.g. vascular lesion or a tumour.

Sensory ataxia is differentiated from cerebellar ataxia in Table 1.158.

**Romberg's Sign**

It is a sign of sensory ataxia. It is said to be positive if a person can stand without swaying when eyes are open but tends to sway when eyes are closed.

It is negative in cerebellar lesions as person tends to sway with eyes open as well as closed.

False positive Romberg's sign may occur in hysteria.

**661. What is vertiginous ataxia?**

Vertiginous (labyrinthine) ataxia is a disorder of gait associated with vertigo, dizziness and light-headedness. The causes of labyrinthine ataxia are due to involvement of labyrinth;

- Acute labyrinthitis
- Meniere's disease
- Vestibular neuronitis
- Streptomycin-induced

Vertiginous ataxia resembles cerebellar ataxia except that vertigo and dizziness accompany the former but not the later.

Labyrinthine ataxia also occurs more when the eyes are open than when the eyes are closed. Romberg's signs is negative

**662. Name the ataxias in which Romberg's sign is negative.**

- Ans.**
- Cerebellar ataxia
  - Vertiginous ataxia
  - Labyrinthine ataxia

**663. What are the signs suggestive of posterior column involvement?**

**Ans.** Following are the signs:

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### 1. *Sensory disturbances*

- Girdle-like sensation at the level of compression
- Deep sensations (sense of position, vibration), fine touch (light touch, two-point discrimination and sense of localisation, stereognosis, graphesthesia etc) are lost.
- Superficial sensations, e.g. pain, touch (crude) and temperature are preserved
- Romberg's sign is positive
- Lhermitte's sign is positive

### 2. *Motor disturbances*

- Loss of coordination, e.g. sensory ataxia
- Tone is diminished
- Power normal

### 3. *Reflexes*

- Deep tendon jerks absent but superficial reflexes preserved
- Plantars are flexor
- No bladder or bowel disturbance



**CASE 49: MYOTONIA**

A 50 years male presented with weakness of distal groups of muscles of extremities. He also complained of frontal baldness and abnormal facial appearance and dysarthria. Examination revealed wasting of distal muscles, myotonia (poor hand - grip relaxation), bilateral ptosis and cataract (Figs 1.49A and B).



**Figs 1.49A and B:** Myotonia dystrophica. A. Note the frontal baldness, abnormal facial appearance and dysarthria. B. Note the wasting of small muscles of hand

**664. What is the probable clinical diagnosis?**

**Ans.** Presence of myotonia (disturbed tone) along with wasting of distal muscles in a 50-year male who presented with frontal baldness, abnormal facial expression and dysarthria suggest the diagnosis of *dystrophic myotonia*.

**665. What is myotonia? What are its type?**

**Ans.** Myotonia is defined as continued muscle contraction with poor relaxation after the cessation of voluntary effort. Myotonias are inherited disorders (autosomal dominant).

The inherited rare types of myotonias are;

1. Myotonia dystrophica
2. Myotonia congenita (Thomsen's disease)
3. Proximal myotonic myopathy. It is characterised by myotonia in middle aged persons with proximal muscle weakness and cataract. It is also inherited as autosomal dominant.

**666. What is clinical significance of myotonia?**

**Ans.** These patients of myotonia tolerate the anaesthesia poorly, hence, it is essential to recognise them.

**667. What are the clinical characteristics of dystrophia myotonica (mytonia dystrophica)?**

**Ans.** It is an autosomal dominant condition characterised by;

- Late age of onset (20-50 years)
- Progressive distal muscle weakness
- Bilateral ptosis
- "Hatchet-face appearance" due to atrophy of temporalis, masseter, sternomastoid and facial muscles (Fig. 1.49A)
- Dysarthria due to weakness of palatal, pharyngeal and tongue muscles
- Myotonia can be demonstrated by percussion over the tongue, thenar eminence and wrist extensor muscles. There is delayed hand-grip relaxation.
- Other associated features;
  - Frontal baldness
  - Cataract
  - Mental retardation
  - Cardiomyopathy and conduction defects
  - Hypogonadism and small pituitary fossa
  - Glucose intolerance
  - Low serum IgG.

**668. What is myotonia congenita?**

**Ans.** This is also an autosomal dominant disorder, milder form occurs in childhood and persists throughout life. Severe form occurs in infants of affected mothers and characterised by facial and bulbar muscle weakness and respiratory insufficiency and mental retardation.

This myotonia is accentuated by rest, cold and is more noticeable on starting the activity following prolonged rest. There may be diffuse hypertrophy of the muscles. Strength is well preserved.

**669. How do you test temporalis and sterno-mastoids?**

**Ans.** Read "Clinical Methods in Medicine" Vol. I.

**670. How will you demonstrate myotonia at the bed side?**

**Ans.** The methods of demonstration are:

1. *Hand grip*: There is poor relaxation of hand grip during shaking hand with the patient.
2. *Percussion*: Percussion over the thenar eminence produces a dimple which disappears (relaxes) slowly.

Similarly percussion over the tongue produces the same above phenomenon.

3. *Slow relaxation of eye after closure*. Ask the patient to close the eyes forcibly, and now ask him to open the eyes. The patient opens the eyes slower than normal.

**671. How will you investigate such a case?**

**Ans.** Investigations are:

- *Serum CK level*. It may be normal or mildly elevated
- *EMG (electromyography)*. It is diagnostic, shows high frequency waxing and waning discharges and a myopathic pattern.
- *Muscle biopsy*. It shows type I fibres with increased numbers of central nuclei, ring fibres and sarcolemmal masses.

**672. Name the drugs useful in myotonia?**

**Ans.** Drugs used in myotonia are:

- Phenytoin
- Quinine
- Procainamide
- Mexiletine.

**CASE 50: MYOPATHY**

A 6-year M (Fig. 1.50A) presented with progressive weakness of muscles of lower limbs and difficulty in walking and in climbing stairs. There was history of difficulty in running and boarding a bus. Patient has no history of mental changes. There was no history of bowel and bladder disturbances. There was no respiratory and cardiovascular complaints.

Examination revealed pseudohypertrophy of the calf muscles and Gower's sign was positive. The knee and ankle jerks were diminished. Plantars were flexor. Sensory system was normal. Respiratory and cardiovascular systems were essentially normal.



**Fig. 1.50A:** Duchenne muscular dystrophy

**673. What is your probable diagnosis and why?**

**Ans.** The muscle weakness, pseudohypertrophy of calves, positive Gower's signs, loss of tendon reflexes in the lower limbs with normal plantars with no sensory involvement suggest the diagnosis of a primary muscle disorder, i.e. myopathy. In view of his age of onset and positive family history the child has Duchenne type of myopathy.

**674. What is myopathy?**

**Ans.** Myopathy (muscular dystrophy) is defined as genetically determined primary degeneration of muscle fibres without an evidence of involvement of central or peripheral nervous system.

**675. How do you classify myopathies?**

**Ans.** The myopathy being hereditary disorders are classified on the basis of inheritance (Table 1.159).

**Table 1.159:** Classification of hereditary myopathies

**I. X-linked**

- *Duchenne type* (severe type of pseudohypertrophic muscular dystrophy)
- *Becker type* (milder form with pseudohypertrophy)

**II. Autosomal recessive**

- Limbs girdle (e.g. scapulohumeral or pelvi-femoral)
- Congenital muscular dystrophy

**III. Autosomal dominant**

- Facioscapulohumeral (Landouzy- Dejerine type)
- Scapuloperoneal
- Oculopharyngeal or ocular
- Distal myopathy

**676. What are the characteristic features of Duchenne type of muscular dystrophy?**

**Ans.** Male child presents with difficulty in climbing stairs and getting up from sitting position. Other features are:

- Positive family history
- Slow onset and progressive disease
- Mental retardation (may be present)
- Positive Gower's sign
- Pseudohypertrophy of the calves and atrophy of other limb muscles
- Jerks may be normal or diminished
- Normal sensory system and sphincter control
- No fasciculations
- Waddling gait

**677. What are similarities and dissimilarities between Duchenne and Becker muscular dystrophies?**

**Ans.** These are given in Table 1.160.

**678. What are the differences between pseudohypertrophy and true hypertrophy (hypertrophic musculorum vera) of muscles?**

**Ans.** These are given in Table 1.161.

**679. What are the causes of pseudohypertrophy of muscles?**

**Ans.** Causes are:

- Duchenne muscular dystrophy (DMD)
- Myxoedema (hypothyroidism)

**Table 1.160** Similarities and dissimilarities between Duchenne and Becker type of myopathy

<b>Similarities</b>		
<ul style="list-style-type: none"> <li>Both are X-linked (mutation of dystrophin gene), progressive myopathies</li> <li>Positive family history</li> <li>Positive Gower's sign</li> <li>Presence of pseudohypertrophy</li> <li>EMG and muscle biopsy findings</li> <li>Treatment protocol</li> </ul>		
<b>Dissimilarities</b>		
Feature	Duchenne type	Becker type
<ul style="list-style-type: none"> <li>Age of onset</li> <li>Severity</li> <li>Mental retardation</li> <li>Cardiomyopathy and ECG abnormalities</li> <li>Kyphoscoliosis</li> <li>Respiratory involvement</li> <li>Prognosis</li> </ul>	<ul style="list-style-type: none"> <li>Infancy or childhood</li> <li>Severe</li> <li>Common</li> <li>Common</li> <li>Common</li> <li>Early</li> <li>Death occurs before second decade</li> </ul>	<ul style="list-style-type: none"> <li>Adolescence or adult onset</li> <li>Mild</li> <li>Uncommon</li> <li>Uncommon</li> <li>Uncommon</li> <li>Late</li> <li>Death before second decade is rare</li> </ul>

**Table 1.161:** Pseudohypertrophy vs true hypertrophy

Pseudohypertrophy	True hypertrophy
<p>Muscle bulk is due to deposition of fibrofatty tissue</p> <p>Muscles are doughy to feel (elasticity is lost)</p> <p>Muscles are firm and globular on contraction</p> <p>The muscles are weak and hypotonic in spite of bulky size</p> <p>Muscles showing pseudohypertrophy are; calf muscles, glutei, quadriceps, deltoids and infraspinati. Tongue muscles may be involved</p>	<p>Muscle bulk is due to increase in muscle mass</p> <p>Muscles are soft and elastic</p> <p>Muscles are hard and globular on contraction</p> <p>The muscles are stronger than normal</p> <p>Muscles showing true hypertrophy include calf muscles or glutei and quadriceps</p>

- Glycogen storage disease
- Trichinosis

**680. Which muscles are not involved in Duchenne muscle dystrophy?**

**Ans.** The muscles spared in DMD are; facial and small muscles of hand.

**681. What are the causes of true hypertrophy of muscle?**

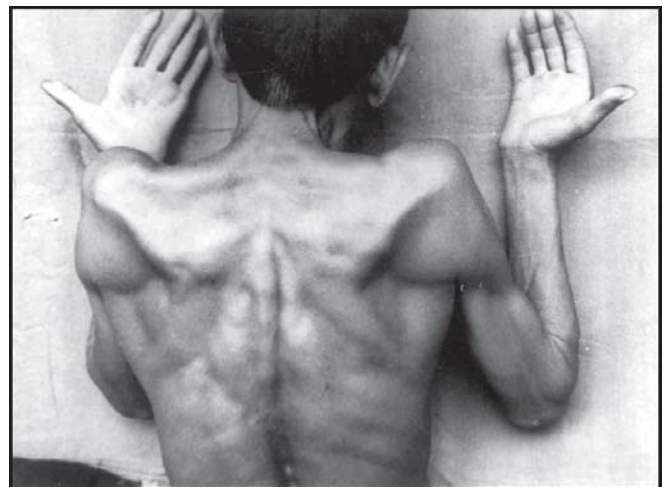
**Ans.** Causes are:

- Labourers (manual hard work)
- Athletes
- Myotonia
- Cysticercosis in the muscles
- Hypertrophic musculorum vera (a rare inherited disorder).

**682. What is limb girdle myopathy?**

**Ans.** Limb girdle myopathy transmitted as autosomal dominant or recessive inheritance, is characterised by

muscle weakness of pelvic and shoulder girdle muscles (Fig. 1.50B). It affects both males and females in the age groups of 10-40 years. Diaphragm may be involved



**Fig. 1.50B:** Fascioscapulohumeral myopathy. Note the wasting of shoulder girdle muscles leading to winging of scapulae

producing respiratory insufficiency. The disease is progressive and varies from family to family. Cardiac involvement (cardiomyopathy) may lead to CHF or arrhythmias. CK levels are elevated. EMG and muscle biopsy reveal myopathic pattern.

**683. What are the causes of proximal muscle weakness?**

**Ans.** The causes of proximal muscle weakness (myopathy) are:

- Muscular dystrophies
- Collagen vascular disorders, e.g. polymyositis
- Diabetic amyotrophy
- Endocrinal myopathy, e.g. cushing's syndrome, thyrotoxicosis
- Metabolic myopathies, e.g. hypokalaemic
- Porphyria
- Guillain-Barré syndrome
- Myasthenic- myopathic syndrome
- Drug-induced, i.e. steroid, triamcinolone
- Paraneoplastic syndrome

**684. What are the causes of distal muscle weakness?**

- Distal myopathy of Gower
- Charcoat-Marie-Tooth disease
- Familial polyneuropathy or acquired polyneuropathy
- Myotonia dystrophica
- Guillain-Barré syndrome (postinfective)
- Chronic inflammatory demyelinating polyneuropathy (CIDP).

**685. What is Gower's sign? What are conditions in which Gower's sign is positive?**

**Ans.** When the patient is asked to stand from lying down, he adopts a peculiar manner of rising – called Gower's rising sign or Gower's sign. To demonstrate this sign, the patient (child) is asked to sit on the floor and then rise. In rising from the floor, the affected child gets up first on his hands and knees (see Fig. 1.50A), brings the legs close to the arms, then "climbs up" the legs to the erect position.

*Significance:* This sign indicates just the proximal (pelvic girdle) muscle weakness, hence, is not specific for Duchenne muscular dystrophy (DMD). It may be present in following conditions.

- Proximal myopathy involving legs (pelvic girdle) due to any cause
- Myasthenia gravis with proximal limb muscles involvement
- Polymyositis
- Spinal muscular dystrophy
- Endocrinal myopathy

**686. What is Waddling gait?**

**Ans.** It is akin to the "gait of a duck". In this type of gait, patient walks on a wide base and sways from side to side during walking. The heels and toes are brought down simultaneously. There is increase in lumbar lordosis. It indicates the proximal muscle weakness and is seen in proximal myopathy. The other causes are:

- Duchenne muscular dystrophy
- Advanced pregnancy
- Bilateral dislocation of hips
- Osteomalacia
- Sometimes huge ascites.

**687. What is winging of scapulae?**

**Ans.** This is lifting off the scapula from the chest when patient attempts abduction and forward movement, e.g. pressing against a wall in standing position. This is due to weakness of scapular stabiliser muscles, is seen in facioscapulohumeral myopathy (Fig. 1.50B).

**688. What is oculopharyngeal myopathy?**

**Ans.** It is an autosomal dominant disorder, characterised by;

- Late onset (5th or 6th decade)
- Ptosis (bilateral), external ophthalmoplegia (limitation of eye movements with sparing of pupillary reaction for light and accommodation).
- Diplopia is not a feature
- Dysphagia resulting in pooling of secretions and repeated episodes of aspiration
- There may be involvement of facial, neck and limb muscles (occasional)

**689. What are causes of bilateral ptosis?**

**Ans.** Read clinical methods in Medicine Vol. I.

**690. What are the causes of muscle wasting?**

- Ans.**
- LMN lesion
  - UMN lesion with disuse atrophy



**Table 1.162:** Myasthenia vs oculopharyngeal myopathy

<b>Myasthenia</b>	<b>Oculopharyngeal myopathy</b>
<ol style="list-style-type: none"> <li>1. An autoimmune disorder (anticholinergic receptors antibodies present)</li> <li>2. Can occur in any age group</li> <li>3. Common in females</li> <li>4. Defect lies in neurotransmission at neuromuscular junction</li> <li>5. Muscle weakness is intermittent, worsened by repetitive use and relieved by rest and anticholinergics</li> <li>6. Bilateral ptosis with diplopia</li> <li>7. Exacerbations and remissions common</li> <li>8. Facial muscles and muscles of mastication are commonly involved. Limb muscles are also involved</li> <li>9. Thymoma may be associated</li> <li>10. Repetitive nerve stimulation (reduction in the amplitude of evoked response) and anticholinergic receptors antibodies tests are positive and diagnostic</li> <li>11. Steroids, immunosuppressive drugs, thymectomy, plasmapheresis and IV immunoglobulins are therapeutic options</li> </ol>	<ul style="list-style-type: none"> <li>• Heredofamilial disorder</li> <li>• Commoner in younger age</li> <li>• Occurs in both sexes</li> <li>• Defect lies in the muscles (intrinsic muscle disease)</li> <li>• Weakness is stationary and progressive</li> <li>• Bilateral ptosis without diplopia. Progressive external ophthalmoplegia is presenting feature</li> <li>• Slowly progressive disease</li> <li>• They are rarely or occasionally involved. Involvement of limb muscles is uncommon</li> <li>• No link with thymoma</li> <li>• EMG and muscle biopsy are specific but anticholinergic receptor antibodies are absent</li> <li>• No treatment, hence, no therapeutic option</li> </ul>

- Muscular dystrophies
- Disseminated malignancy (malignant cachexia)
- Diabetes mellitus
- Thyrotoxicosis
- Advanced malnutrition or debility
- Anorexia nervosa

### 691. How will you investigate a case of myopathy?

**Ans.** Following investigations are helpful;

- *CK (creatinine kinase) enzyme serial estimation.* The levels are increased
- *EMG* shows myopathic pattern
- Muscle biopsy confirms the diagnosis by showing changes of muscle degeneration and regeneration without any cellular infiltration. There is decreased level of dystrophin in the muscles demonstrated by immunochemical staining (Western blot)

- *ECG changes* are present if cardiac muscle is involved (cardiomyopathy). These include tall R waves in  $V_1$  and  $V_2$ , deep Q waves in  $V_5$ - $V_6$  and RBBB.

*Note:* Read testing of individual muscle in clinical methods in medicine vol. 1 by Prof SN Chugh.

### 692. What is myasthenia gravis? How does it differ from oculopharyngeal myopathy?

**Ans.** Myasthenia gravis is an autoimmune disorder of neuromuscular junctions characterised by weakness and fatiguability of muscles worsened by repetitive use with a tendency to recover with rest and anticholinergic drugs. The underlying defect is a decrease in the number of acetylcholine receptors (AChRs) at neuromuscular junctions due to antibody-mediated autoimmune attack.

The differences between myopathy and myasthenia gravis are given in Table 1.162.

### CASE 51: WASTING OF SMALL MUSCLES OF HAND AND CLAW HANDS

The patient (30M) presented with thinning of palms of the hands without pain, paraesthesias or numbness along with weakness of both the lower limbs. There was history of widespread twitchings of the muscle. There was no history of bowel and bladder disturbance. Examination revealed wasting of thenar and hypothenar eminence with clawing of hands. The knuckles and bony prominences of hands were prominent. There was hollowing of dorsal interosseous spaces. No trophic changes or sensory loss. Upper limb reflexes were exaggerated despite wasting. In the lower limbs. There were exaggerated deep tendon reflexes with ankle clonus. Plantars were bilateral extensors.



**Fig. 1.51:** Wasting of small muscles of hands

#### 693. What is the probable diagnosis and why?

**Ans.** The probable diagnosis is motor neuron disease. The points in favour of the diagnosis are:

1. Wasting of small muscles of hands with exaggerated reflexes in upper limbs despite wasting
2. Diffuse widespread twitchings (fasciculations)
3. UMN type of quadriplegia (spastic quadriplegia)
4. No sensory loss or trophic changes.

#### 694. What are the causes of wasting of small muscles of hands?

**Ans.** The involvement of lower motor neuron in the upper limbs from its origin (anterior horn cells) to its end

(muscle) can produce wasting of small muscles of the hand. Depending on the site of involvement, the causes are divided into various groups:

#### I. Diseases involving the anterior horn cells (AHC)

- Poliomyelitis
- Motor neuron disease (amyotrophic lateral sclerosis)
- Syringomyelia
- Intramedullary tumours (gliomas, ependymoma)

#### II. Diseases involving motor (anterior) nerve roots (radiculopathy)

- Leptomeningitis
- Arachnoiditis (patchy)
- Cervical spondylosis
- Neuralgic amyotrophy

#### III. Lesions in brachial plexus

- Birth injury (Klumpke's paralysis – C<sub>8</sub>-T<sub>1</sub>)
- Cervical rib
- Thoracic inlet-syndrome

#### IV. Peripheral nerve lesions

- Peripheral neuropathy
- Peroneal muscular atrophy involving the upper limbs also
- Carpal tunnel syndrome
- Median and ulnar nerve palsy due to injuries

#### V. Diseases of the muscles

- Distal myopathy (early and late onset)
- Myotonia dystrophica
- Volkmann's ischaemic contractures
- Muscular ischaemia due to peripheral vascular disease

#### VI. Disuse atrophy (reflex wasting, Sudeck's atrophy)

- Rheumatoid arthritis
- Post-paralytic (UMN paralysis)
- Post-fracture

#### VII. As a part and parcel of systemic wasting

- Malignancy, diabetes, thyrotoxicosis, tuberculosis and nutritional
- Paraneoplastic.

#### 695. Which nerve roots supply small muscles of hands?

**Ans.** C<sub>8</sub> and T<sub>1</sub> nerve roots

#### 696. How will you test small muscles of hands?

**Ans.** Read "Clinical methods in Medicine Vol.I"

**697. What are the causes of fasciculations?**

Ans. Read "Clinical methods in Medicine Vol. I"

**698. How do you diagnose a cervical rib clinically?**

Ans. The cervical rib is suspected clinically when the patient complains of pain along the ulnar border of the hand and forearm. Examination reveals sensory loss in the distribution of T<sub>1</sub> with wasting of the thenar muscles. Horner's syndrome may occur. The Adson's test is positive.

*Adson's test:* This is positive in cervical rib and thoracic outlet syndrome. The examiner feels the pulse of sitting patient by standing behind the patient. Now patient is instructed to turn the head on the affected side and asked to take deep breath. The pulse either get diminished or obliterated on the side affected during this manoeuvre.

**699. Name the muscles of thenar and hypothenar eminence.**

Ans. Following are the muscles:

<i>Muscles of thenar eminence</i>	<i>Muscles of hypothenar eminence</i>
• Abductor pollicis brevis	• Abductor digiti minimi
• Flexor pollicis brevis	• Flexor digiti minimi
• Opponens pollicis	• Opponens digiti minimi

**700. What is claw hand? What are its causes?**

Ans. Read case discussion on peripheral neuropathy.

Paralysis of interossei and lumbricals produce *claw hand*.

**701. What is wrist drop?**

Ans. Read case discussion on peripheral neuropathy.

**702. What are trophic changes? Name the trophic changes in skin?**

Ans. Trophic changes are neurogenic in origin, involve skin, its appendages and joints (Charcot joint), occur due to repeated trauma in the region of anaesthesia.

The trophic changes in the skin include;

- Dry and rough skin with lack of sweating
- Pigmentation
- Fall of hairs (hypotrichosis)
- Local cyanosis or oedema
- Nails are brittle
- Trophic ulcers.

**703. What are sites of trophic changes? What are its causes?**

Ans. Trophic changes are common at pressure points such as:

- On the lateral malleolus
- Back of heel of the foot/feet
- Over the sacrum (classical site for bed sore)
- Back of shoulder girdle.

The causes are same as that of Charcot joint.

**704. What is Charcot joint? What are its causes?**

Ans. It is a neuropathic joint characterised by:

- Painless joint swelling (e.g. knee, hip, shoulder joint)
- Hypermobile joint
- Disorganised and destroyed joint
- Loose bodies or osteophytes in the joint cavity
- Palpable crepitus

*The causes of Charcot's joint are:*

- Peripheral neuropathies, commonly due to leprosy, diabetes and hereditary sensory neuropathy
- Syringomyelia (upper limb joints are commonly involved)
- Tabes dorsalis (lower limb joints are commonly involved)

For Charcot joint, always test for the sensations.

**705. How will you arrive at the aetiological diagnosis of wasting of small muscles of hands?**

Ans. History and physical examination will help to find out the cause of wasting of small muscles of hand.

1. *History:* Wasting since childhood is common with poliomyelitis and birth injury (Klumpke's paralysis)
2. Ask for *neck pain*: It occurs in cervical spondylosis, cervical rib and intra or extramedullary tumour
3. Fasciculations with brisk tendon reflexes in the case described above indicate amyotrophy lateral sclerosis
4. Symmetrical joint involvement - Rheumatoid arthritis
5. Trophic changes in hands -, e.g. leprosy, syringomyelia, cervical rib
6. Thickened ulnar nerve - leprosy
7. No sensory loss indicates motor neuron disease while dissociated sensory loss indicates syringomyelia.

**CASE 52: ALOPECIA**

A female patient (Fig. 1.52) presented with loss of hair on the scalp. Examination showed patchy loss of hair on the scalp.



**Fig. 1.52:** Alopecia areata. A young female with non-scarring loss of scalp hair

**706. What is the most likely diagnosis?**

**Ans.** • Alopecia areata is probable diagnosis. Sudden onset of patchy hair loss in an adult suggests alopecia areata.

**707. What is alopecia areata?**

**Ans.** It is probable an autoimmune disorder involving, skin, hair, and nails causing patchy nonscarring alopecia with pitting, ridging and furrowing of nails.

**708. What is alopecia totalis and alopecia universalis?**

**Ans.** If all the hair on the scalp are lost, it is called alopecia totalis, and if there is complete loss of body hair, it is called alopecia universalis.

**709. What are the causes of alopecia?**

**Ans.** These are given in Table 1.163.

**710. What are the sites of alopecia areata?**

**Ans.** The sites are:

1. Scalp
2. Beard, eyebrows and eyelashes
3. Moustache.

**711. What is pathognomonic sign of alopecia areata?**

**Ans.** The presence of “exclamation mark hair” at the periphery of lesion is the pathognomonic sign.

**Table 1.163:** Causes of alopecia

**I. Nonscarring alopecia**

- A. Primary cutaneous disorders
  - Telogen effluvium
  - Androgenic alopecia
  - Alopecia areata
  - Tinea capitis
  - Traumatic alopecia
- B. Drugs, e.g. Thallium, heparin, anti-metabolites, hypervitaminosis
- C. Systemic diseases
  - SLE
  - Secondary syphilis
  - Hypo and hyperthyroidism
  - Deficiency of proteins, biotin and Zn
  - HIV infection

**II. Scarring alopecia**

- A. Primary cutaneous disorders
  - Cutaneous lupus
  - Lichen planus
  - Folliculitis decalvans
  - Linear scleroderma (morphea)
- B. Systemic diseases
  - SLE
  - Sarcoidosis
  - Cutaneous metastases

**712. Which systemic disorders are associated with alopecia areata?**

**Ans.** Alopecia areata being an immune-mediated non-inflammatory disorder is associated with other autoimmune disorders such as:

- Autoimmune thyroid disorders
- Vitiligo
- Pernicious anaemia
- Atopy

**713. What is the commonest cause of alopecia.**

**Ans.** Alopecia areata.

**714. Name the commonest systemic disorder producing alopecia.**

**Ans.** SLE

**715. What is treatment of alopecia areata?**

**Ans.** • Minoxidil  
• Psoralens with UVA/UYA sol (topical and systemic) and steroids (topical and systemic).

**716. What is trichotillomania?**

**Ans.** It is mechanical pulling of hair leading to broken hair.

**Table 1.164:** Diagnosis and differential diagnosis, pathogenesis and treatment of various nonscarring alopecia including alopecia areata

Condition	Clinical features	Pathogenesis	Treatment
<i>Alopecia areata</i>	<ul style="list-style-type: none"> <li>Well-circumscribed patchy areas of hair loss, 2-5 cm in diameter</li> <li>Extensive involvement may lead to hair loss on other hair-bearing surfaces of the body</li> <li>Nail pitting, ridges, and furrows can be seen</li> </ul>	<ul style="list-style-type: none"> <li>The germinal zones of the hair follicles are surrounded by T-lymphocytes leading to cessation of hair growth and club-hair formation</li> <li>Hereditary (Down's syndrome), stress, endocrinal and other autoimmune disorders like Addison's disease, hyper and hypothyroidism, vitiligo, pernicious anaemia may be associated</li> </ul>	<ul style="list-style-type: none"> <li>Topical anthralin, intralesional and systemic steroids, topical contact sensitizer</li> </ul>
<i>Telogen effluvium</i>	<ul style="list-style-type: none"> <li>Sudden diffuse shedding off normal hairs</li> <li>Causes include certain major stresses, e.g. pregnancy, postpartum, acute severe infection, acute psychiatric illness, emotional or physical trauma</li> <li>Reversible without treatment</li> </ul>	Stresses cause the normally asynchronous growth cycles of individual hair to become synchronous, therefore large number of growing hairs (anagen) simultaneously enter the dying (telogen) phase	<ul style="list-style-type: none"> <li>No treatment required</li> <li>Only observation</li> <li>Discontinue the offending drug</li> <li>Check thyroid functions</li> </ul>
<i>Androgenic alopecia</i> (common male baldness)	<ul style="list-style-type: none"> <li>Symmetric diffuse hair loss in fronto-central (midline) area of the scalp</li> <li>Recession of anterior, posterior and lateral hair lines in all men and some women</li> </ul>	<ul style="list-style-type: none"> <li>Increased sensitivity of affected hairs to testosterone</li> <li>Increased levels of circulating androgens (ovarian and adrenal source in women)</li> </ul>	If no evidence of hyper-androgen state then topical minoxidil ± tretinoin; hair transplant or wig wearing on the scalp
<i>Tinea capitis</i>	Hair loss varies from scaling with minimal hair loss to discrete patches with black dots (broken hairs) to boggy plaque with pustules (kerion)	Invasion of hairs by dermatophytes	<ul style="list-style-type: none"> <li>Oral griseofulvin plus 2.5% selenium sulphide or ketoconazole shampoo</li> <li>Examine other family members</li> </ul>
<i>Traumatic alopecia</i>	<ul style="list-style-type: none"> <li>Broken hairs</li> <li>Irregular outline</li> </ul>	<ul style="list-style-type: none"> <li>Traction with curlers, rubber bands, braiding</li> <li>Exposure to heat or chemicals</li> <li>Mechanical pulling (trichotillomania)</li> </ul>	<ul style="list-style-type: none"> <li>Discontinue the offending hair style or chemical treatment</li> <li>Hair clipping and psychotherapy for trichotillomania</li> </ul>

**717. What is differential diagnosis of alopecia areata?**

**Ans.** All the causes of nonscarring alopecia (primary

cutaneous disorders) come into the differential diagnosis and pathogenesis of alopecia areata is tabulated (Table 1.164).



**CASE 53: ERYTHEMA NODOSUM**

The patient presented with bilateral painful small nodules over the skin after taking some drug. There was associated history of fever and arthralgia. The nodules were tender and palpable (Fig. 1.153).



**Fig. 1.53:** Erythema nodosum over the skin

**718. Describe the skin lesions. What is your clinical diagnosis?**

- Ans.**
- The lesions are multiple, red erythematous nodules which are non-itchy but painful and tender
  - They are bilateral and symmetrical (only one side is shown)
  - They are present on the shin

The probable clinical diagnosis is Erythema Nodosum.

**719. What is erythema nodosum? What is common site of this lesion?**

**Ans.** Erythema nodosum is a panniculitis (inflammation of fat) characterised by painful, tender, subcutaneous, red (erythematous) nodules. The lesions are present on the extensor surfaces, e.g. anterior portion of leg (over the shin), thigh, upper arm or forearm.

Shin is the commonest site

**720. What are the common causes of erythema nodosum?**

- Ans.** Common causes are:
- Primary pulmonary tuberculosis

- Infections, e.g.  $\beta$ -hemolyticus streptococci, yersinia, salmonella and chlamydia
- Lepromatous leprosy
- Inflammatory bowel disease, e.g. ulcerative colitis or Crohn's disease
- Sarcoidosis
- Drug hypersensitivity, e.g. sulphonamides, penicillins, oral contraceptives and barbiturates
- Fungal infections, e.g. histoplasmosis or coccidioidomycosis
- Behcet's syndrome
- Brucellosis
- Rarely in rheumatic fever.

**721. What is basic pathology of the lesion?**

**Ans.** This is type III (immune complex) hypersensitivity reaction, involves the fat (panniculitis) and the blood vessels (vasculitis).

The shin is the commonest site of involvement because foreign proteins and bacteria are slowly removed from the "front of the legs" due to poor lymphatic drainage.

**722. What are other common skin lesions over the shin?**

- Ans.** In addition to erythema nodosum, other lesions are:
- Pretibial myxoedema (a feature of Graves' dermopathy)
  - Necrobiosis lipoidica diabetorum (seen in diabetes)
  - Lichen amyloidosis.

**723. What is erythema nodosum leprosum?**

**Ans.** Read the question on lepra reactions in leprosy.

**724. What are the causes of red (erythematous), subcutaneous nodules?**

**Ans.** Causes are:

1. Inflamed epidermal inclusion cysts, acne cysts and furuncles
2. Panniculitis due to any cause. The various forms of presentation of panniculitis are;
  - Erythema nodosum
  - Erythema induration/nodular vasculitis
  - Lupus profundus (seen in lupus vulgaris)

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- Weber-Christian disease
  - Alpha-1-antitrypsin deficiency
  - Fat necrosis due to pancreatic disease
  - Factitious
3. Cutaneous/systemic vasculitis
    - Polyarteritis nodosa
    - Allergic granulomatosis
    - Wegener's granulomatosis
  4. Cutaneous metastases

### 725. What is Panniculitis?

**Ans.** It is inflammation of subcutaneous fat, characterised by tender nodules either singly or in multiple crops.

#### Causes

- Collagen vascular disorders
- Lymphoma
- Pancreatitis
- NB. Erythema nodosum is a common example of panniculitis

### 726. What is vasculitis? What are its causes?

**Ans.** Vasculitis is inflammation of the blood vessels, can be due to:

1. Infections
2. Drugs
3. Immunological diseases, e.g. SLE, dermatomyositis, systemic sclerosis, rheumatoid arthritis, polyarteritis nodosa, Wegener's granulomatosis
4. Malignant diseases.

### 727. What are cutaneous manifestations of vasculitis?

**Ans.** The cutaneous features are:

1. *Erythema*, e.g. generalised rash, palmar erythema, erythema multiforme, erythema nodosum
2. *Purpura*, e.g. purpuric spots, palpable purpura
3. *Dactylitis*, *digital ulceration*, *gangrene*.

### 728. What is small vessel vasculitis? Name various conditions associated with small vessel vasculitis.

**Ans.** Involvement of small vessels in vasculitic process is called *small vessel vasculitis*. It is commonly ANCA associated vasculitis. The conditions are:

1. Churg-Strauss syndrome
2. Microscopic polyangitis
3. Wegener's granulomatosis
4. Anaphylactoid purpura
5. Hypersensitivity (cutaneous) vasculitis
6. Essential cryoglobulinaemic vasculitis.

### 729. What is erythema multiforme? What are its causes? What is Stevens-Johnson's syndrome?

**Ans.** Erythema multiforme is an abnormal cutaneous vascular reaction to a number of stimuli.

The causes of erythema multiforme are:

1. Herpes simplex viral infection
2. Bacterial (streptococcus, mycoplasma) infection
3. Fungal infection, e.g. histoplasmosis
4. Parasitic infestations
5. Drugs, e.g. sulphonamides, barbiturates
6. Systemic diseases, e.g. SLE, lymphoreticular malignancies
7. Pregnancy.

**Stevens-Johnson's syndrome** is severe or major form of erythema multiforme characterised by erosions of skin and mucous membrane with haemorrhagic crusting, may lead to shock or hypotension creating an emergency situation in dermatology.

### 730. What is Behcet syndrome?

**Ans.** It is a syndrome of recurrent oro-genital mucocutaneous ulceration of unknown aetiology. Systemic manifestations involving the eyes, joints, brain may also occur. The mucocutaneous lesions are treated by colchicine or thalidomide while systemic manifestations require steroids or anti-mitotic drugs.

**CASE 54: HYPERPIGMENTATION**

A male 25 years presented with diffuse hyperpigmentation (Fig. 1.54). There was no history of loose motion and weakness. Examination revealed normal BP with pigmentation of hands and tongue. There were no signs of nutrients or vitamins deficiency.



**Fig. 1.54:** Hyperpigmentation. Note the black pigmentation of face, tongue and hands

**731. What is your diagnosis?**

**Ans.** Hyperpigmentation, probably idiopathic.

**732. What is hyperpigmentation? What are its causes?**

**Ans.** Abnormal increased pigmentation is called *hyperpigmentation* which may be localised (due to skin disorders) or generalised (due to systemic disorders).

The localised forms are due to increased epidermal alteration, melanocytes proliferation, or an increased melanin production. The generalised forms occur due to darkening of the skin usually of equal intensity over the entire body or pigmentation may be accentuated in the sun-exposed areas. The causes of hyperpigmentation are tabulated (Table 1.165).

**733. What are the sites to be seen for hyperpigmentation?**

**Ans.** Sites of inspection are:

- Face
- Inside the buccal cavity especially inner sides of cheeks (commonly for Addison's disease,

**Table 1.165:** Causes of hyperpigmentation

**I. Localised**

- (i) *Epidermal alteration*
  - Seborrhoeic keratosis
  - Acanthosis nigricans
- (ii) *Proliferation of melanocytes*
  - Lentigo, systemic diseases, e.g. Peutz-Jeghers, LEOPARD syndromes, xeroderma pigmentosa
  - Melanoma
  - Nevus, NAME and LAMB syndromes
- (iii) *Increased melanin production*
  - Ephelides (freckles)
  - Café-au-lait spots

**II. Generalised**

- (i) *Endocrinopathies*
  - Addison's disease. Nelson's syndrome
  - Ectopic ACTH production. Cushing's syndrome
- (ii) *Metabolic*
  - Porphyria cutanea tarda
  - Hemochromatosis
  - Vit B<sub>12</sub> and folate deficiency
  - Pellagra
  - Malabsorption, whipple disease
- (iii) *Autoimmune*
  - Biliary cirrhosis
  - Scleroderma, SLE
  - POEM syndrome
- (iv) *Melanosis secondary to metastatic melanoma*
- (v) *Drugs and metals*
  - Minocycline, cancer chemotherapy, clofazimine, psoralens, bleomycin
  - Heavy metals, e.g. gold, arsenic, silver and lead

malabsorption, Peutz-Jegher's syndrome) and palate

- Palmar creases (Addison's disease)
- General skin over pressure points, scar, palms and soles

**734. What is kala-azar? What is the type and site of pigmentation?**

**Ans.** Kala-azar (Hindi version "black fever") is caused by *Leishmania*, hence called *leishmaniasis*.

The skin lesions including hyperpigmentation develop in some patients during or within a few months of therapy (e.g. in East Africa) or years after therapy (e.g. in India). The lesions are pigmented macules, papules, nodules or patches typically seen over the face around the mouth, on the temple and forehead. Persons with skin lesions act as reservoirs of infections.

**735. What is Addison's disease?**

**Ans.** Read Addison's disease as a separate case.

**736. What are the sites of pigmentation in Addison's disease?**

**Ans.** Sites are:

1. Pressure points (elbow)
2. Normally pigmented areas (areola, genitalia, knuckles, palmar creases and scars)
3. Mucous membranes (mouth).

**737. What do you understand by hemochromatosis? What is the site and type of pigmentation in this disease?**

**Ans.** Hemochromatosis is a common disorder of iron storage in which inappropriate increase in iron absorption from the intestine results in excessive iron deposition into the parenchymal cells of liver, pancreas, heart and pituitary leading to their dysfunction. The characteristic feature of the disease are;

- Autosomal recessive disorder
- Excessive skin pigmentation, e.g. bronze pigmentation
- Diabetes mellitus (bronze diabetes)
- Cardiac involvement, e.g. cardiomyopathy, CHF
- Hepatic enlargement (cirrhosis of liver, hepatocellular carcinoma in advanced disease)
- Arthropathy
- Hypogonadism, e.g. loss of libido, testicular atrophy

Skin pigmentation is called *bronze pigmentation*, occurs due to excessive deposition of melanin and iron, gives a metallic or slate grey hue to the skin. The pigmentation is diffuse and generalised but may be more pronounced on the face, neck, extensor surfaces of lower forearms, dorsum of the hand, lower legs, genitalia and in scars.

**738. What is Peutz-Jegher's syndrome?**

**Ans.** It is heritable (autosomal dominant) disorder characterised by polyposis of small intestine and colon with mucocutaneous (circumoral) pigmentation and tumours of the ovary, breast, pancreas and endometrium. The chances of malignant transformation of polyposis are rare.

**739. What is chloasma or melasma?**

**Ans.** This is symmetrical hyperpigmentation seen on malar prominences and bridge of the nose mostly in young females (very rare in males) precipitated by pregnancy (chloasma gravidarum) or following prolonged use of oral contraceptives – called *mask of pregnancy*.

**740. What is malar flush? What is plethoric face?**

- Read malar flush in mitral stenosis (mitral facies).
- The plethoric or suffused or congested face is discussed in Cushing's syndrome and SVC obstruction.

**741. Name the syndromes associated with localised hyperpigmentation (lentigines)?**

**Ans.**

1. LEOPARD syndrome
  - L stands for lentigines (localised multiple hyperpigmentation)
  - E stands for ECG abnormalities (conduction defects)
  - O for ocular hypertelorism
  - P stands for pulmonary stenosis and aortic stenosis
  - A stands for abnormal genitalia (cryptorchidism, hypospadias)
  - R stands for retardation of growth
  - D stands for deafness – sensorineural

**2. NAME and LAMB syndromes**

Localised pigmentation, e.g. lentigines are associated with atrial myxomas in two syndromes, i.e. NAME (Naevus, Atrial myxoma, Myxoid neurofibroma and Ephelidis) and LAMB (Lentigines, atrial myxoma, Mucocutaneous myxomas and Blue naevi). These patients can have endocrinopathies in the form of Cushing's syndrome, acromegaly or sexual precocity.

**742. What is lentigines? How do they differ from freckles?**

**Ans.** Lentigines are light brown or dark brown macules of varying sizes (1 mm-10 mm), discrete and present on any part of the body. The differences between freckles and lentigines are given in the Box 1.5.

**Box 1.5: Freckles vs lentigines**

<i>Freckles</i>	<i>Lentigines</i>
<ul style="list-style-type: none"> <li>• Individuals are fair-skinned</li> <li>• Located to photoexposed areas</li> <li>• Variable in colour, e.g. light to dark</li> <li>• Darken on exposure to sunlight</li> </ul>	<ul style="list-style-type: none"> <li>Any skin colour</li> <li>Any part of the skin and even mucosa</li> <li>Each lesion is of uniform colour</li> <li>No change in colour</li> </ul>

**743. What are endocrinal causes of pigmentation?**

**Ans.** See the Table 1.165.

**744. Name the drugs producing pigmentation.**

**Ans.** See the Table 1.165.



**CASE 55: LEPROSY**

A patient presented with few hypopigmented anaesthetic macules (Fig. 1.55A) with loss of hair and dryness. On examination, ulnar nerves were palpable and firm to feel. No other organomegaly.



**Fig. 1.55A:** Leprosy

**745. What is probable clinical diagnosis and why?**

**Ans.** Tuberculoid leprosy. The palpable nerves with hypopigmented anaesthetic patches are characteristic features of T. leprosy.

**746. How is it caused? What is mode of transmission?**

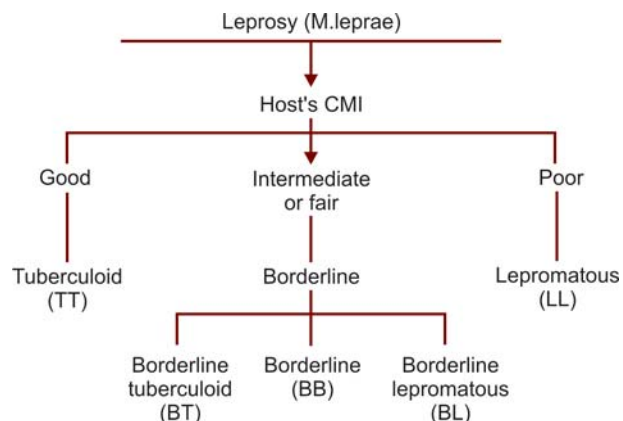
**Ans.** It is caused by *Mycobacterium leprae* – a gram-positive acid-fast and alcohol – fast bacillus-called **Hansen's bacillus**.

**Mode of Transmission**

Man is only reservoir of infection, hence, untreated patients with extensive disease (smear positive) are potential source of transmission to healthy persons. The routes of transmission are; nasal (aerosol) and oral while skin contact may also be a mode if lesion is ulcerated. Foamites and vectors do not play any role in its transmission.

**747. How do you classify leprosy? What are its different clinical types?**

**Ans.** Depending on the cell-mediated immunity (CMI), the leprosy is classified into two polar forms and a borderline form (Fig. 1.55B).



**Fig. 1.55B:** Clinical types of leprosy depending on host immune status/CMI

**Note:** Lepromatous leprosy means multibacillary (highly bacillated), low resistance with systemic disease; while tuberculoid leprosy means paucibacillary, high resistance with localised disease.

**748. What are the clinical features of leprosy?**

**Ans.** Three common clinical types are compared in Table 1.166. Incubation period is 3-5 years.

**749. What are systemic manifestations of leprosy?**

**Ans.** The systemic manifestations are common only in lepromatous leprosy due to low resistance/CMI. The manifestations are;

1. Hepatosplenomegaly/lymphadenopathy
2. Nephrotic syndrome
3. Symmetric peripheral neuropathy with gloves and stocking type of anaesthesia
4. Granulomatous uveitis and keratitis
5. *Leonine facies* (Fig. 1.55C): The features are;
  - Lines on the forehead become deeper as well as upper central incisor teeth loosen or may fall. There is hoarse voice.
  - Loss of hair on lateral thirds of eyebrows and thickened eyebrows.
  - Saddle deformity of nose

**Table 1.166:** Clinical features of three common types of leprosy

Feature	Tuberculoid (TT)	Borderline (BB)	Lepromatous (LL)
• No. of lesion	One to three	Many	Numerous
• Distribution	Localised	Widespread asymmetrical	Generalised symmetrical
• Size of lesion	Large	All sizes	Small lesions
• Margin/edge	Well defined	Ring lesions	Vague
• Surface	Dry and hair loss present	Some dry, some smooth	—
• Sensation over lesion	Impaired	Larger lesion may have impaired sensation	Impaired sensation over periphery
• Type of sensory loss	Localised	Localised	Glove and stocking type of anaesthesia (peripheral neuropathy)
• Nerves (nerve twigs or peripheral nerves)	Limited, thickened and may be palpable	Many regional nerves thickened	Symmetrical peripheral neuropathy with trophic changes
• Hepatosplenomegaly / lymphadenopathy	Absent	May or may not be present	Present usually
• Skin smear	Negative	Negative /positive	Positive
• Lepromin test	Highly positive	Just positive	Negative

**Fig. 1.55C:** Lepromatous leprosy. Note the typical face in this type of leprosy

- Perforation of nasal septum
- Thickened skin of face due to massive infiltration especially ear lobes

6. Testicular atrophy and gynaecomastia
7. Anaemia, e.g. haemolytic, megaloblastic or iron deficiency.

**750. What are causes of thickened peripheral nerves?****Ans.** Causes are:

- Leprosy

- Amyloidosis
- Diabetic neuropathy
- Sarcoidosis
- Charcoat-Marie – Tooth disease
- Idiopathic hypertrophic neuropathy
- Neurofibromatosis
- Acromegaly
- Post-Guillain-Barre syndrome
- Dejerine–Sottas type neuropathy or Refsum's disease

**751. What are conditions that produce leonine-like face?****Ans.** Causes are:

- Albright's disease
- Carcinoid syndrome
- Amyloidosis
- Cleidocranial dysostosis
- Primary hypertrophic osteoarthropathy
- B-cell lymphoma

**752. What are complications of leprosy?****Ans.** Complications are:

- Crippling deformities
- Blindness

- Tuberculosis
- Secondary amyloidosis
- Social stigma

### 753. What is lepromin test? What is its significance?

**Ans.** Lepromin is suspension of autoclaved *M. leprae* obtained from human or armadillos. 0.1 ml is injected intradermally and test result is read after 48-72 hours (Fernandez reaction) and 4 weeks (Mitsuda reaction). Fernandez reaction represents the delayed hypersensitivity while Mitsuda reaction represents cell-mediated immunity (CMI).

The test is strongly positive in tuberculoid leprosy, just positive in borderline tuberculoid and negative in lepromatous. In borderline it is weakly positive and negative in borderline lepromatous.

### 754. What is borderline leprosy?

**Ans.** The borderline portion of the leprosy spectrum (Fig. 1.50B ) lies between the tuberculoid and lepromatous poles and is further subdivided into;

- Borderline tuberculoid (BT)
- Borderline or dimorphous (BB)
- Borderline lepromatous (BL)

Classification within the borderline region is less precise than at the poles. Lesions tend to increase in number and heterogeneity but decrease in individual size as the lepromatous pole is reached. The skin lesions of borderline tuberculoid leprosy generally resemble those of tuberculoid disease but are more numerous and less well defined. Involvement of multiple peripheral nerve trunks are more common than in polar tuberculoid leprosy.

The borderline disease states are unstable and may shift towards lepromatous form in untreated patient or toward the tuberculoid pole during treatment. Change of one polar type to other is rare.

### 755. What are various reactions in leprosy?

**Ans.**

1. *Type I lepra reaction (reversal reaction)*. It can complicate all the three borderline (BB, BT, BL) types, existing skin lesions develop erythema and swelling, new lesions may appear and the nerves become

tender. It is managed by aspirin, corticosteroid and chloroquine.

2. *Type II Lepra reaction or erythema nodosum leprosum (ENL)*.

It occurs in lepromatous (LL) or borderline lepromatous (BL) patients. It occurs in patients in their second year of treatment. Tender, inflamed subcutaneous nodules develop in crops with pain in the nerves. Fever, arthritis, lymphadenopathy may accompany severe ENL. Each nodule lasts for a week or two but new crops may continue to appear.

It is treated by analgesics, antipyretics, thalidomide (contraindicated in pregnancy) or steroid and increasing the dose of clofazimine.

ENL develops due to immune-mediated (immune complex) reaction.

3. *Lucio phenomenon*. It is characterised by arteritis, is limited to patients with diffuse infiltrative non-nodular lepromatous leprosy. The patients develop angular ulcers. It is a complication rather than reaction.

### 756. What are disabilities/deformities in leprosy?

**Ans.** These are given in Table 1.167

### 757. What is differential diagnosis of leprosy?

**Ans.** A D/D of skin lesion are as follows:

*The skin lesion in leprosy* has to be differentiated from other conditions given below. The hypoaesthetic lesion and involvement of peripheral nerve trunks in the areas involved are characteristics of leprosy.

- SLE
- Lupus vulgaris (tuberculosis of skin)
- Sarcoidosis
- Yaws
- Dermal leishmaniasis

### 758. What is claw hand? What are its causes?

**Ans.** *Claw hand (main-en-griff)*: is a condition where the metacarpophalangeal (MCP) joints are hyperextended and the PIP and DIP joints are flexed.

Claw hand is produced by paralysis of interossei and lumbricals (small muscles of hand)

**Table 1.167:** Disabilities/ deformities in leprosy

Site	Nerve	Disability	Deformities if any
Face	Facial nerve Trigeminal	<ul style="list-style-type: none"> <li>Lagophthalmos (inability to close the eyes)</li> <li>Corneal anaesthesia</li> </ul>	Exposure keratitis Exposure keratitis and blindness
Hand	Ulnar	<ul style="list-style-type: none"> <li>Clawing of 4th and 5th fingers</li> <li>Anaesthesia over the little and inner half of ring finger</li> </ul>	Deformities of these fingers
	Median nerve	<ul style="list-style-type: none"> <li>Loss of abduction and apposition of thumb</li> <li>Anaesthesia over the thumb, index, middle and outer half of ring finger</li> </ul>	Deformities of these fingers
	Ulnar and median	<ul style="list-style-type: none"> <li>Claw hand</li> <li>Loss of sensations over the whole palm</li> </ul>	Claw hand deformity and contracture
	Radial	<ul style="list-style-type: none"> <li>Wrist drop</li> <li>Loss of sensations and sweat over the back of hand</li> </ul>	<ul style="list-style-type: none"> <li>Contractures</li> <li>Ulceration</li> </ul>
Foot	Common peroneal and lateral popliteal Posterior tibial	<ul style="list-style-type: none"> <li>Foot drop</li> <li>Anaesthesia over lower leg and dorsum of foot</li> <li>Claw toes</li> <li>Anaesthesia and loss of sweat over the sole of foot</li> </ul>	<ul style="list-style-type: none"> <li>Contractures</li> <li>Trophic ulcers on the leg</li> <li>Contractures of toes</li> <li>Trophic ulceration</li> </ul>

The causes and differential diagnosis of claw-hand include;

1. Combined lesion of ulnar and median nerve by injury or leprosy
2. Cervical rib or thoracic inlet syndrome involving lower trunk of brachial plexus
3. Klumpke's paralysis
4. Motor neuron disease
5. Syringomyelia and intramedullary tumours.

### 759. What is differential diagnosis of peripheral neuropathy?

**Ans.** Read case discussion on peripheral neuropathy.

### 760. How do you diagnoses leprosy?

**Ans.** Diagnosis is based on clinical examination and investigations such as,

1. *Slit skin smear stained with modified Ziehl-Neelsen method* to detect the lepra bacillus at a concentration  $>10^4$  /g of tissue. Bacteriological index (number of bacilli living or dead) is calculated on 6 points logarithmic scale.

Bacteriological Index in LL is 5-6

Bacteriological index in TT is 0

The morphological scale (MI) of smear (% of all bacilli that stain solidly indicating living bacilli) is also calculated. This confirms the diagnosis.

2. *Skin biopsy*: It is done where diagnosis is in doubt and to classify the disease accurately.
3. *Nerve biopsy*: It is done in pure neuritic leprosy.
4. *Lepromin test*
5. *Sweat function test* by pilocarpine or acetylcholine. Loss of sweat indicate leprosy.
6. *Fluorescent leprosy antibody absorption (FLA-ABS)* test to detect *M. lepra* specific antibody.
7. *ELISA* for antibody.
8. *Polymerase chain reaction (PCR)*.

### 761. How do you treat leprosy?

**Ans.** The WHO and NLEP regimens for treatment of paucibacillary (tuberculoid, borderline tuberculoid and indeterminate classes) and multibacillary (borderline lepromatous, lepromatous leprosy and indeterminate classes) leprosy are tabulated (Table 1.168).

### Side Effects of Anti-leprosy Drug:

1. Clofazimine – red colouration of skin, urine and body secretions, abdominal pain, anorexia, nausea, vomiting, pruritus

**Table 1.168:** WHO and NLEP regimens for leprosy

Group	Drugs	Adult dose (mg)	Regimen	Duration
1. Paucibacillary (PB), i.e. BT, BB and TT	<ul style="list-style-type: none"> <li>• Rifampicin</li> <li>• DDS</li> </ul>	600 100	One monthly supervised Daily self-administered	6 monthly pulses to maximum of 9 month
2. Multibacillary (MB), i.e. BL, LL	<ul style="list-style-type: none"> <li>• Rifampicin</li> <li>• Clofazimine</li> <li>• Dapsone</li> <li>• Clofazimine</li> </ul>	600 300 100 50	Once monthly supervised Daily self-administered	12 monthly pulses to maximum of 18 months

2. Dapsone – exfoliative dermatitis, hemolytic anemia, agranulocytosis, hepatitis, psychosis and hypoproteinaemia.

**762. What are uses of rifampicin (bactericidal drug)?**

**Ans.**

- Tuberculosis and other atypical mycobacterial infection
- Leprosy
- For prophylaxis of meningococcal meningitis
- Legionnaires' disease
- Brucellosis (given alongwith other drugs)
- Eradication of carrier state of typhoid (along with co-trimoxazole)
- Endocarditis (*Staph. aureus*, *Corynebacterium*). It is given along with vancomycin.

**763. Name the other drugs used in leprosy. What is the possibility of vaccine in leprosy?**

**Ans.** Other drugs used are;

- Acedapson (DADDS)
- Ethionamide
- Thiocetazone
- Thiobutosine
- Minocycline
- Ofloxacin

**Vaccine:** Attempts have been made to achieve quicker control of leprosy after the drugs have killed the lepra bacilli. For this various agents like BCG and mycobacterial vaccine (BCG + killed *M. lepra*, killed ICRC vaccine and kill M.W.) are being tried.



**CASE 56: RAYNAUD'S PHENOMENON**

The patient presented with episodes of pain and paraesthesias of the finger-tips followed by changes in the colour of the skin (Fig. 1.56). Examination revealed cyanosis of the fingers without clubbing. On symptomatic enquiries, patient admitted paleness before bluishness of fingers and after sometimes there was return of normal skin colour on rubbing the fingers. There was no evidence of digital gangrene.



**Fig. 1.56A:** Raynaud's phenomenon. Note the bluish fingers of left hand. Pulse was normal. This was the second phase of tricolour response of Raynaud's phenomenon

**764. What is your clinical diagnosis?**

**Ans.** The episodic nature of change in colour of the skin from pale to blue (cyanosis) and then red (rubor) without any digital gangrene indicates vasospastic disorder probably Raynaud's phenomenon.

**765. What is Raynaud's phenomenon?**

**Ans.** Raynaud's phenomenon is characterised by episodic vasospasms of digital arteries leading to sequential development of tricolour response (digital blanching, cyanosis and rubor) of the fingers or toes following cold exposure and subsequent return on rewarming.

In this phenomenon, patient experiences pallor or whiteness of fingers or toes when exposed to cold environment or touching a cold object. Emotional stress precipitates this phenomenon.

**766. What is pathophysiology of Raynaud's phenomenon?**

**Ans.** Raynaud's phenomenon is cold-induced episodic digital ischemia secondary to reflex sympathetic vasoconstriction or an enhanced vascular responsiveness to cold or normal sympathetic stimuli.

The tricolour response and its pathogenesis is described in Table 1.169.

**767. How do you classify Raynaud's phenomenon?**

**Ans.** It is divided into two categories:

1. Raynaud's disease. It is idiopathic where no cause is known.
2. Secondary Raynaud's phenomenon. It is secondary to some identifiable or known cause.

**768. What is Raynaud's disease?**

**Ans.** It is primary idiopathic Raynaud's phenomenon. The term is used when the secondary causes of Raynaud's phenomenon have been excluded, hence, it is diagnosed by exclusion.

It affects young females (20-40 years); and is confined to fingers more frequently than toes. Examination is entirely normal. Peripheral (radial, ulnar and pedal) pulses are normal.

**Table 1.169:** Tricolour response in Raynaud's phenomenon

Colour	Mechanism
Pallor or whiteness	Digital ischemia due to vasoconstriction
Bluishness (cyanosis)	Local capillaries and venules dilate and cyanosis results from deoxygenated blood present in these vessels
Redness (Rubor)	Resolution of vasospasm and reactive hyperaemia due to vasodilatation and return of blood flow imparts a bright red colour to the digits
Note: Although tricolour response is characteristic of Raynaud's phenomenon but some patients may experience only pallor and cyanosis or only cyanosis	

The patients tend to have attacks of pain and paraesthesias with tricolour response which resolves completely in most of the cases or may improve spontaneously in about 15 per cent cases; while in 30 per cent cases it may progress.

**769. What are the causes of secondary Raynaud's phenomenon?**

**Ans.** The causes are given in Table 1.170.

**Table 1.170:** Causes of Raynaud's phenomenon

1.	<b>Collagen vascular disorders</b>
	• Scleroderma
	• SLE
	• Rheumatoid arthritis
	• Dermatomyositis and polymyositis
2.	<b>Occlusive arterial disease</b>
	• Atherosclerosis of peripheral vessels
	• Thromboangiitis obliterans (Buerger's disease)
	• Thoracic outlet syndrome
3.	<b>Primary pulmonary hypertension</b>
4.	<b>Neurological disorders</b>
	• Intervertebral disc disease
	• Syringomyelia
	• Spinal tumours
	• Poliomyelitis
	• Stroke
	• Carpal tunnel syndrome
5.	<b>Blood dyscrasias</b>
	• Myeloproliferative disorders
	• Cryoglobulinaemia
	• Waldenström's macroglobulinaemia
	• Cold agglutinins
6.	<b>Trauma</b>
	• Mechanical injury, e.g. typing, piano-playing, vibration, etc.
	• Cold injury
	• Hammer hand syndrome
	• Electric shock
7.	<b>Drug-induced</b>
	• Ergot derivatives, methysergide, betablockers, bleomycin, vinblastine, cisplatin

**770. What are the six common causes of Raynaud's phenomenon?**

**Ans.**

1. Raynaud's disease (idiopathic)
2. Collagen vascular diseases, e.g. SLE, scleroderma
3. Primary pulmonary hypertension
4. Cold injury
5. Myeloproliferative disorders, e.g. leukaemia
6. Thoracic outlet syndrome.

**771. What is treatment of Raynaud's phenomenon?**

**Ans.** Most of the patients have mild attacks, do not need treatment except reassurance and protection of the body from exposure to cold by warm clothings, gloves and socks.

- Drug treatment: It is indicated in severe cases. The calcium channel blockers, e.g. nifedipine (10-30 mg tds) and diltiazem (30-90 mg tds) decrease the frequency and severity of attacks. Postsynaptic alpha blockers, e.g. prazosin (1-5 mg tds), doxazosin and tetrazosin may be effective. Long-term use of reserpine (0.25-0.5 mg q.i.d.) therapy is not recommended due to adverse effects.

Treatment with vasodilator prostaglandins is under investigation.

- Surgical sympathectomy is helpful in those cases who are resistant to medical therapy.

**772. What is scleroderma? What are its type and manifestations?**

**Ans.** **Scleroderma** – also called *systemic sclerosis* is a multisystem disorder of unknown aetiology characterised by inflammatory, vascular and fibrotic changes in the skin, blood vessels and internal organs (chiefly GI tract, heart, lungs, and kidneys). Immunological mechanism leading to vascular damage and stimulation of fibroblasts are considered responsible for it.

**Types**

1. *Diffuse cutaneous scleroderma*. It involves skin of proximal and distal extremities, face and trunk. Visceral involvement occurs in early course of the disease.
2. *Limited cutaneous scleroderma or CREST syndrome* It is characterised by **Cal**cinosis, **R**aynaud's phenomenon, **E**sophageal dysmotility, **S**clerodactyly and **T**elangiectasia. Skin involvement is limited to face and extremities distal to elbows. It has better prognosis. Clinical manifestations are tabulated (Table 1.171)  
Diagnosis is based on clinical manifestations, physical examination (especially of face and extremities) and confirmation is done by skin biopsy (Table 1.172).

**773. Name the localised form of scleroderma.**

**Ans.** Localized forms are:

- CREST syndrome

**Table 1.171:** Clinical manifestations of scleroderma

<b>1. Cutaneous</b>
<ul style="list-style-type: none"> <li>• Raynaud's phenomenon with puffy finger (90% cases) is the presenting manifestation</li> <li>• Thickening of skin which is tightly bound to underlying subcutaneous tissues, e.g. extremities, face and trunk</li> <li>• Mat-like telangiectasia</li> <li>• Calcinosis cutis on pressure points</li> </ul> <p>These features constitute CREST syndrome</p>
<b>2. Musculoskeletal</b>
<ul style="list-style-type: none"> <li>• Symmetrical polyarthrititis</li> <li>• Carpal tunnel syndrome</li> <li>• Proximal muscle weakness or myopathy</li> </ul>
<b>3. GI tract</b>
<ul style="list-style-type: none"> <li>• Esophageal hypomotility (e.g. heart burn, GERD, dysphasia)</li> <li>• Intestinal hypofunction, e.g. pseudo-obstruction, malabsorption, chronic constipation</li> </ul>
<b>4. Pulmonary</b>
<ul style="list-style-type: none"> <li>• Aspiration pneumonia/alveolitis</li> <li>• Fibrosis or interstitial lung disease</li> <li>• Restriction of chest movements (hidebound chest)</li> <li>• Hypertension, it may lead to cor pulmonale</li> </ul>
<b>5. Cardiac</b>
<ul style="list-style-type: none"> <li>• Pericarditis</li> <li>• Cardiomyopathy (restrictive)</li> <li>• Conduction defects /arrhythmias</li> <li>• Hypertension and left ventricular failure</li> </ul>
<b>6. Renal</b>
<ul style="list-style-type: none"> <li>• Hypertension</li> <li>• Renal failure</li> </ul>

- Morphea (single or multiple plaques of skin induration)
- *En coup de sabre* (e.g. linear scleroderma of one side of face. It may be associated with facial hemiatrophy).

**774. What is mixed connective tissue disease (MCTD)?**

**Ans.** It is an *overlap syndrome* comprising of features of SLE, scleroderma, polymyositis and rheumatoid arthritis. It is accompanied by high titres of circulating antibodies to nuclear ribonucleoprotein (NRNP) antigen.

**775. What is differential diagnosis of scleroderma?**

**Ans.**

1. Read the differential diagnosis of Raynaud's phenomenon
2. Read vasculitis in case discussion on erythema nodosum.

**776. What is treatment of systemic sclerosis (scleroderma)?**

**Ans.** The treatment is as follows:

1. Regular exercises to maintain flexibility of the limbs
2. *Drug treatment*
  - D-penicillamine (diminishes cross-linkage collagen)

**Table 1.172:** Physical sign in scleroderma

<b>Face in scleroderma</b>
<ul style="list-style-type: none"> <li>• Expressionless (mask-like) face</li> <li>• Absence of normal skin wrinkling</li> <li>• Pinched out nose or beaking of nose</li> <li>• Microstomia</li> <li>• Telangiectation of fingers, face, lips, tongue etc.</li> <li>• Inability to open the mouth</li> <li>• Skin is glossy and shiny</li> <li>• Pigmentation and depigmentation</li> </ul>
<b>Hands in scleroderma</b>
<ul style="list-style-type: none"> <li>• Sclerodactyly, e.g. skin is thick and tight bound on the fingers and cannot be lifted (Fig. 1.56B)</li> <li>• Symmetrical puffy fingers</li> <li>• Limitation of movements (extension and flexion of fingers) leading to contractures</li> <li>• The fingertips may lose soft tissue (pulp atrophy) and develop digital ulcers (Fig. 1.56B) and scars</li> <li>• Skin is dry, coarse but shiny with loss of hairs</li> <li>• Nail fold changes include thrombi</li> <li>• Digital 'infarcts and gangrene</li> <li>• Pseudoclubbing may be present due to bone resorption of terminal phalanx</li> </ul>



**Fig. 1.56B:** Systemic sclerosis. Sclerodactyly with stellate fingertip ulcers

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- Colchicine (inhibits procollagen conversion to collagen)
- PABA
- Vitamin E
- Dimethyl sulphoxide

### 3. Symptomatic treatment

- For reflex oesophagitis (use mosapride or itopride)
- For myositis – use steroids
- For articular symptoms – use NSAIDs
- Antibiotics for infection
- ACE inhibitors for hypertension

### 4. Treatment of Raynaud's phenomenon- already described.

#### 777. What are the uses of Colchicine?

**Ans.** Uses are:

- Acute gout
- Scleroderma
- Primary biliary cirrhosis

- Amyloidosis
- Psoriasis
- Familial Mediterranean Fever
- Chromosomal study
- Behcet's syndrome
- Myelofibrosis

#### 778. Name the drugs that produce scleroderma like illness.

**Ans.** Drugs are:

- Bleomycin
- Vinylchloride
- Pentazocine

#### 779. What is systemic sclerosis sine scleroderma?

**Ans.** Systemic sclerosis in which there is visceral involvement only without Raynaud's phenomenon or other skin manifestations is called *systemic sclerosis sine scleroderma*.

### CASE 57: SUBCUTANEOUS SWELLINGS/MASSES

A patient (Fig. 1.57) presented with subcutaneous swellings (arrows), nontender which are present diffusely on the body. Examination revealed rubbery multiple swellings located along the distribution of peripheral nerves under the skin which can be moved from side to side but not from above downwards. There was no evidence of pigmentation, hypertension or deafness. There was positive family history. The patient even brought his son for the examination and treatment of these swellings.



**Fig. 1.57:** Neurofibromatosis. Note the multiple subcutaneous swellings. Family history was positive in this case

#### 780. What is the clinical diagnosis in this case and why?

**Ans.** The multiple subcutaneous swellings along the peripheral nerves, soft in consistency, nontender, moving from side to side only, indicate subcutaneous neurofibromas.

#### 781. What are the causes of subcutaneous swellings?

**Ans.** The causes are:

- Neurofibromatosis
- Rheumatoid nodules
- Rheumatic nodules
- Leprosy
- Cysticercosis

- Xanthomas
- Lipomas, fibromas
- Calcinosis
- Osler's nodes
- Gouty tophi
- Skin metastases from carcinomas
- Panniculitis (erythema nodosum)

#### 782. What do you understand by neurofibromas?

**Ans.** Neurofibromas are multiple benign tumours of the peripheral nerves, comprising of Schwann cells and fibroblasts. They are fixed to the nerves from which they arise, hence, can only be moved from side to side. They are soft, usually nontender (sometimes painful and tender) and exhibit the “button-hole” sign, i.e. they invaginate into the skin with pressure.

#### 783. What is neurofibromatosis? What are its types?

**Ans.** Neurofibromatosis is an inherited autosomal dominant condition characterised by neurofibromas and pigmented lesions of the skin, e.g. *café-au-lait spots* and phakomatosis (collection of neuroglial tissue) of retina.

**Types**

1. *Neurofibromatosis type I (von Recklinghausen's disease)* is peripheral type of neurofibromatosis. Mutation of the neurofibromatosis gene I (NF1) causes it. The gene is situated on chromosome 17 that encodes a protein called *neurofibromin*. The features of the disease are;
  1. Multiple cutaneous or subcutaneous neurofibromas
  2. Compressive radioculopathy or neuropathy
  3. Café-au-lait spots (> 6 in number and > 1.5 cm in diameter)
  4. Hemartomas of iris (Lisch nodules)
  5. Axillary freckling
  6. Pseudoarthrosis of tibia
  7. Hydrocephalus, sclerosis, short stature, hypertension (pheochromocytomas), epilepsy and mental retardation may occur.
2. *Neurofibromatosis type 2.* It is central type of neurofibromatosis. Mutation of gene NF<sub>2</sub> causes it. The gene is situated over the chromosome 22 that encodes a protein called *neurofibromin 2*,



*Schwannomin* or *merlin*. The features of this type of disease are:

1. Bilateral acoustic Schwannomas
2. Predisposition to development of meningiomas, gliomas and Schwannomas
3. Cataract (juvenile posterior subcapsular lenticular opacity)
4. Multiple café-au-lait spots
5. Peripheral neurofibromas.

**784. What are the common causes of café-au-lait spots?**

- Neurofibromatosis
- Albright's disease (polyostotic fibrous dysplasia)
- Tuberous sclerosis
- Ataxia telangiectasia
- Multiple endocrine adenomatosis type III
- Occasionally occur normally usually <3 in number
- Watson's syndrome (neurofibromatosis with pulmonary stenosis)

Café-au-lait spots are commonly seen on the trunk.

**785. What are the common sites of cutaneous neurofibromas? What is plexiform neurofibromatosis?**

**Ans.** Sites of cutaneous neurofibromatosis are;

- Sides of the neck
- Extremities

Plexiform neurofibromatosis refers to diffuse overgrowth of the skin and subcutaneous tissue leading to large folds of the skin. The common sites are temple, upper eyelids and back of the neck. Elephantiasis *neurofibromatosa* is severe form of this variety involving the lower limbs.

**786. What is pachydermocele?**

**Ans.** It is a variety of neurofibromatosis in which coils of soft tissue hang around the neck.

**787. What is phakomatoses? What are conditions associated with it?**

**Ans.** Phakomatoses include a group of genetic disorders in which a variety of developmental abnormalities involve the skin, nervous system, retina and other organs. The causes are;

1. von Recklinghausen's disease
2. Von Hippel-Lindau syndrome
3. Multiple endocrine neoplasia I (Werner's syndrome)
4. Retinoblastoma
5. Tuberous sclerosis
6. Sturge-Weber disease
7. Turcot's syndrome

These are also called congenital or hereditary neurocutaneous syndromes.

Phakoma is seen as a greyish circular mass about the size of the half of the disc in the retina and is produced by collection of abnormal glial tissue

**788. What is xanthomas and xanthelasma? What are their causes?**

**Ans.** Xanthomas are yellow-coloured cutaneous papules / nodules or plaques, commonly associated with hyperlipidaemia (hypertriglyceridemia), occur mainly on the extensor surfaces of the extremities and buttocks.

**Types of Xanthomas**

**I. Planus xanthomas**

- Xanthelasma on the eyelids
- Tendinous xanthomas seen on achilles and extensor finger tendon
- Plane xanthomas seen on palmar creases, face, upper trunk and scars

**II. Tuberous xanthomas.** They are seen over the large joints (elbow, wrist, knee, ankle) and buttocks. They are seen in patient's with hypercholesterolemia due to prolonged cholestasis.

*Common causes of xanthomas*

- Familial hyperlipidaemia and hypercholesterolemia
- Biliary cirrhosis or prolonged cholestasis
- Uncontrolled diabetes mellitus
- Multiple myeloma or monoclonal gammopathy
- Hypothyroidism
- Nephrotic syndrome or chronic renal failure
- Obesity
- Drug induced hyperlipidaemia

**789. What do you understand about gouty tophi?**

**Ans.** Tophi are yellow – coloured, firm, small swellings that, occur in gout due to deposition of crystals of

monosodium urate in the skin around the joints particularly of the hands and feet. Other sites of tophi are;

- Helix of the ear
- Olecranon and prepatellar bursae
- Achilles tendon
- Ulnar surface of forearm
- Other pressure points.

Diagnosis is confirmed by demonstration of urate crystals in the aspirated contents of a lesion under polarised light. Urate crystals are needle-shaped and negatively birefringent.

#### 790. What is calcinosis? What are its causes?

**Ans.** Calcinosis cutis is a condition in which insoluble calcium salts are deposited in the dermis. Widespread calcinosis affecting the skin, subcutaneous tissue and the muscles is called *calcinosis universalis*.

In calcinosis, nodule/ plaques are distributed symmetrically over the extremities and trunk.

#### Major Categories of Calcinosis

1. *Dystrophic*. seen in collagen vascular diseases
2. *Metastatic*. This follows hypercalcaemia or hyperphosphataemia

3. *Iatrogenic* due to leakage of calcium salt during injection

4. *Idiopathic*

#### Causes of calcinosis

1. Collagen vascular diseases, e.g. scleroderma, CREST syndrome, dermatomyositis
2. Trauma
3. Post-inflammatory/postinfective
4. Neoplasia.

#### 791. How will you differentiate rheumatoid nodules from rheumatic nodules?

**Ans.** The differences are tabulated (Table 1.173).

#### 792. What is cutaneous cysticercosis?

**Ans.** Cutaneous or muscular cysticercosis produces small, firm nodules in the voluntary muscles anywhere in the body. These nodules are palpable and contain the calcified cyst of *Taenia solium*. Patients are usually pork-eaters and may have features of neurocysticercosis (epilepsy, hydrocephalus, behavioral or mental changes and fluctuating neurological signs).

**Table 1.173:** Distinction between rheumatoid and rheumatic nodules

Features	Rheumatoid nodule	Rheumatic nodule
Size	Large	Small
Locations	Over extensor surfaces of elbow, back of head, over sacrum in bed-ridden patients and extensor tendons of fingers and toes	Situated over the bony prominences or pressure points
Tenderness	Nontender	May be tender
Fixation	Often fixed	Often free
Incidence	Common	Uncommon
Association	Associated with active rheumatoid arthritis (seropositive)	Associated with active carditis (John's criteria)

**CASE 58: SCABIES**

A patient (Fig. 1.58) presented with intense itching of upper limbs, e.g. hands, fingers, forearms, scrotum and groin, worst at night or after a hot bath. Examination revealed, scratch marks over the fingers, arm, forearms, scrotum and groin. Papulo-vesicular lesions were also seen between fingers, axillae, belt line, buttocks, thighs and scrotum.



Fig. 1.58: Scabies

**793. What is probable clinical diagnosis?**

**Ans.** Scabies

**794. How is scabies caused? How does it get transmitted?**

**Ans.** The scabies is caused by infestation by an ectoparasite – *Sarcoptes scabiei*, a human itch mite. Gravid female mites burrow beneath the skin (stratum corneum) for a month, depositing the eggs. Nymphs hatch out from these eggs and mature into adults on the surface of the skin, where they mate and subsequently reinvade the skin of the same or another person.

Transfer of newly fertilized female mites from person to person by intimate personal contact is the mode of transmission of scabies. Medical practitioners are, therefore, at particular risk of infestation.

The crowding, uncleanliness, promiscuity are the precipitating factors. Transmission via sharing of the contaminated bedding, clothing, towel, is infrequent because these mites cannot survive more than a day without host contact.

Outbreaks occur in nursing homes, mental institutions and hospitals.

**795. What is pathognomonic lesion of scabies? What is its characteristic distribution? Which areas are spared?**

**Ans.** *Burrow or tunnel* is the pathognomonic lesion. Burrows appear as dark wavy lines in the epidermis caused by tunnelling of the mite in the skin and end in a small pearly bleb that contains the female mite.

**The Characteristic Distribution of Burrows;**

The areas involved are:

- Webs of the fingers, volar aspect of wrist, ulnar border of forearm and arms, anterior axillary folds
- Scrotum, penis, vulva, groin and medial aspects of thigh and webs of toes

**Areas spared are:**

- Face, scalp, neck, palms and soles.

**796. Name the various lesions in scabies.**

**Ans.** Various lesions are:

- Typical burrows seen as wavy lines
- Small papules and pustules often accompanied by eczematous plaques
- Pustules or nodules
- Crusted scabies and prominent fissuring can occur due to bacteraemia in AIDS patients.

**797. What is non-itchy (Norwegian) scabies?**

**Ans.** Features of non-itchy scabies are:

- *Crusted (or Norwegian) scabies* is a non-itchy scabies. It results from hyperinfestation with thousands or millions of mites; the predisposing conditions being steroids use, immunocompromised state and neurological or psychiatric illness (mentally retarded patients)

**798. Why is the itch nocturnal in scabies?**

**Ans.** The mites need a warm environment to move, hence, when patient retires in a warm bed at night, the mites start moving within the burrows and cause itch.

**799. How do you diagnose scabies?**

**Ans.** The diagnostic clues are:

- Pruritus and polymorphic skin lesions at characteristic locations

- Burrows or comedones
- Itching either nocturnal or occur after a hot bath
- History of involvement of several members of the family due to household contact
- Biopsy or scrapings of papulovesicular lesions for mite, its eggs or fecal matter may also be confirmative.
- Burrows unroofed with a sterile needle or scalpel blade and scrapings taken and transferred to a glass slide on which 10% potassium hydroxide is kept. The slide is then examined under microscope for mite, its eggs or its fecal pellets which confirm the diagnosis.

### 800. Which skin conditions lead to itching?

**Ans.** The conditions are:

- Scabies
- Urticaria
- Lichen planus
- Ringworm
- Psoriasis
- Dermatitis herpetiformis
- Eczematous dermatitis
- Pediculosis
- Insect bite

### 801. What are the medical causes of generalised pruritus?

**Ans.** Medical causes are:

- Cholestasis (obstructive jaundice)
- Chronic renal failure (CRF)
- Polycythemia rubra vera
- Carcinoid syndrome
- Systemic anaphylaxis
- Systemic mastocytosis
- Thyrotoxicosis
- Diabetes mellitus
- Drug – induced
- Psychogenic
- Pregnancy

### 802. What are complications of scabies?

**Ans.** Common complications of scabies are:

- Superinfection, e.g. pyoderma
- Acute glomerulonephritis due to sensitisation to nephrogenic strains of streptococci (superinfection)
- Eczematous dermatitis due to prolonged itching or sensitisation from parasite
- Complication due to treatment, e.g. sulphur dermatitis.

### 803. How do you treat scabies?

- Family contacts to be screened and treated simultaneously
- Secondary infection is treated by antibiotics
- Medicine used and instructions given to the patient are:

*Medicines used:*

1. Twenty-five percent benzylbenzoate
2. Unguentum sulphur
3. Gamma benzene hexachloride (1%) – not to be used in pregnant women and infant
4. Monosulfiram used as soap
5. Topical thiabendazole
6. Permethrin (5% cream)
7. Malathione (0.5%)
8. Ivermectin (200 µg/kg/orally as a single dose). Patients with crusted scabies (Norwegian variety) require two or more doses of ivermectin.

*Method of use*

Patient is advised to take bath with soap and H<sub>2</sub>O. During bath, patient must scrub his body to open the burrows and then allow the skin to dry. Now apply the specific medicine from neck to foot for 3 consecutive days. Patient should take bath daily and wear fresh garments. Clean or autoclave the bed-sheets and used garments.

- Antihistamines and calamine lotion may be used to relieve itching
- Patient's nail should be cut properly. His daily used articles (towel, pillow, bedsheet) to be kept separately.



**CASE 59: PSORIASIS**

The patient (Fig. 1.59) presented with itching and silvery scaly lesion mainly on the extensor surfaces. Scraping or removal of the scales left behind bleeding spots.



**Fig. 1.59:** Psoriasis. Note dry, scaly plaques on the extensor surfaces of extremities and trunk

**804. What is your probable spot diagnosis?**

**Ans.** Psoriasis

**805. What do you understand by psoriasis?**

**Ans.** It is a common chronic inflammatory skin disorder clinically characterised by red erythematous plaques covered with silvery white scales.

**806. What are the characteristics of psoriatic lesion?**

**Ans.** The characteristics of psoriatic lesions are:

1. Classic lesion is a well defined erythematous plaque covered with silvery–white adherent scales
2. The lesions are distributed over the extensor surfaces (e.g. knees, elbows, buttocks), may also involve scalp, hands, palms and soles
3. The skin lesions are pruritic
4. Traumatized areas often develop lesions of psoriasis by local spread (Koebner phenomenon)
5. On grattage, characteristic coherence of scales can be seen as if one scratches a wax candle (*signe de la tache de bougie*)

6. Scrapping or removal of scales leaves behind punctate bleeding spots (*Auspitz's sign*) is diagnostic
7. Associated findings include psoriatic arthritis and nail changes (onycholysis, pitting or thickening of nail plate with accumulation of subungual debris).

**807. What is its aetiology?**

**Ans.** Following are causes:

1. **Genetic basis.** Psoriasis occurs in families (50% patients with psoriasis have positive family history). HLA studies have shown increased frequency of HLA – B13, HLA – B17 and HLA-BW16 in the affected patients. Twin studies report 70% concordance rate among monozygotic twins.
2. **Immunological basis.** Evidence has accumulated indicating a role of T cells in pathophysiology of psoriasis. There is persistent activation of T cells by the antigen as a result of autoreactivity or by the cytokines such as interleukin 2 released from keratinocytes during chemical/physical or UV injury.
3. **Precipitating factors.** Skin trauma, winter season, emotional stress, depression, infection, pregnancy and upper respiratory infection precipitate it.
4. **Drugs.** Beta blockers, NSAIDs, lithium, calcium channel blockers, chloroquine, valproate, carbamazepine, clonidine, penicillin, tetracyclines, glibenclamide and topical coal tar precipitate psoriasis.

**808. What are clinical forms of psoriasis?**

**Ans.** The forms are explained in Table 1.174.

**809. What is psoriatic arthropathy (PA)?**

**Ans.** It is an inflammatory arthritis that occurs in 5 to 10 per cent of patients with psoriasis with negative rheumatoid factor (seronegative arthritis). It is commonly associated with HLA-B 27. Five distinct types recognised are:

1. *Oligoarticular PA.* It is asymmetrical involvement of single or few small joints of fingers. This is commonest type (38%)
2. *Rheumatoid type.* It is symmetrical seronegative arthritis involving the small joints (30%).



**Table 1.174:** Clinical forms of psoriasis

Forms	Clinical characteristics of lesions
Numular	Discoid, coin shaped lesion (commonest form)
Guttate	Drop-like, small sized lesions
Exfoliative	Erythrodermic scaly dermatitis
Pustular (palmo-plantar type)	Superficial pustules containing sterile pus are seen on palms and soles
Generalised pustular (Von Zumbusch psoriasis)	Rare. Generalised pustules with signs of toxæmia, e.g. fever, headache, myalgia are evident
Genital type	Penis and vulva are the site of lesion
Flexural (intertriginous)	Instead of extensor surfaces, flexural sites are affected
Scalp psoriasis	Fairly common, not associated with alopecia
Psoriasis unguis (nail psoriasis)	Onycholysis, pitting of nail plates, subungual hyperkeratosis, yellow discolouration etc.

3. *Classical psoriatic arthropathy*. This is arthritis involving the distal interphalangeal joints (16%)
4. *Psoriatic spondylitis* (Sacroilitis and/or spondylitis). This constitutes 15% cases of PA.
5. *Arthritis mutilans*. Severe destructive arthritis (5%) producing gross deformities of joints of hands and feet.

#### 810. What are the dermatological causes of pitting nails?

**Ans.** Dermatological causes are:

- Psoriasis unguis
- Eczema
- Alopecia areata

#### 811. Name the skin diseases precipitated by trauma (positive Koebner's phenomenon).

**Ans.** These are as follows:

- Psoriasis
- Lichen planus
- Viral warts

#### 812. What are histological changes in psoriasis?

**Ans.** Following are the changes:

- Hyperkeratosis and parakeratosis
- Absence of granular layer
- Hyperplasia of stratum malpighii
- Dilated and tortuous blood vessels in dermal papillae
- Microabscesses of Munro in the horny layer

#### 813. How will you investigate a case with psoriasis?

**Ans.** Following are the investigations:

- TLC, DLC for an evidence of infection
- Rheumatoid factor
- Skin scrapings and nail clippings may be examined for tinea (fungal infection has to be differentiated from psoriasis)
- Skin biopsy. It is rarely required.
- X-rays of hands and feet may show fish tail or "pencil-in-cup" deformity if joints are involved. Subarticular erosions and later cystic destruction of bones may occur. Sacroilitis may occur.

#### 814. What will you treat such a case?

- Ans.**
- Triggering factors should be found out and eliminated
  - Good diet with supplementation of iron and folate
  - Any focus of infection may be treated with antibiotics

A. *Topical treatment*: It consists of;

1. Dithranol (anthralin). It inhibits keratinocytes proliferation by activated T cells and inhibits formation of interleukins. Ingram regimen consists of coal tar bath, exposure to UV rays and application of anthralin (0.1 to 0.8%) in Lassar's paste to psoriatic plaques.
2. Crude coal tar preparation with keratolytic salicylic acid is used as ointment. It may be combined with UV light or anthralin as described above.
3. *Local steroid ointments*
4. *Vitamin D analogue (calcipotriol)* is used locally
5. *Topical preparation* of retinoic acid derivatives (0.1%)

6. Systemic therapy plus/Tazarotene-aretinoid is used as 0.1% gel.

*B. Systemic therapy*

*PUVA therapy.* Administration of psoralens (p stands for Psoralens) and subsequent long wave UVA radiation is called PUVA therapy. Oral psoralens (8 - methoxy psolarens) is followed 2 hours later by UVA therapy. Two to four sittings per week are necessary (total 10-20 sittings). UVB is useful in winter season.

*Other drugs used are:*

1. Methotrexate (2.5-5 mg orally at 12 hours interval, 3 consecutive doses in a week). Cycloporine A may be given 3-5 mg/kg.
2. Mycophenolate Mofetil – an immunosuppressant is used in the dose of 2-3 mg/day
3. Oral Retinoids (etretinate, tretinoin) are used as immuno-modulators in psoriasis. Dose is 0.5-1 mg/kg daily for 4-20 weeks.
4. Oral corticosteroids may be used judiciously in refractory psoriasis, psoriatic arthropathy and in erythrodermic form of psoriasis.
5. NSAIDs are used for arthropathy.

**815. Name the common scaly lesions of skin.**

**Ans.** Common scaly lesions are:

- Psoriasis
- Seborrhoeic dermatitis
- Eczema
- Ringworm
- Pityriasis (all the varieties)
- Lichen planus
- Exfoliative dermatitis.

### CASE 60: PITYRIASIS VERSICOLOR (TINEA VERSICOLOR)

The patient (Fig. 1.60) presented with non-itchy depigmented scaly skin lesions on the back of the chest and side of the neck.



Fig. 1.60: Pityriasis versicolor

#### 816. What is your diagnosis? Describe the skin lesions. How is it caused?

**Ans.** The diagnosis is:

- Pityriasis versicolor

The lesions are well defined hypopigmented macules with fine branny scales of different shapes and sizes. These are non-itchy.

*Sites involved are:*

- Front and back of the chest, side of neck, upper arm and face.

It is caused by *M furfur* – a parasitic form of saprophytic yeast often called *pityrosporum orbiculare*.

#### 817. What are its precipitating factors?

**Ans.** These are as follows:

- Profuse sweating
- Diabetes mellitus
- Pregnancy.

#### 818. How do you confirm the diagnosis?

**Ans.** The diagnosis is confirmed by demonstration of fungal hyphae in the scraped scales treated with KOH (10% solution) taken on a slide and examined under microscope.

#### 819. What are the causes of hypopigmented macules?

**Ans.** Following are the causes:

1. *Tuberculoid leprosy* (the hypopigmented macules are anaesthetic)
2. *Vitiligo* (idiopathic or associated with other autoimmune disease)
3. *Pityriasis alba* and *pityriasis versicolor*
4. *Following burn* (H/o burn)
5. *Tuberous sclerosis* (Shagreen patch). There is history of epilepsy, low intelligence and sebaceous adenoma. It may be familial.
6. *Prolonged use of chloroquine* in rheumatoid arthritis and SLE
7. *Psoriasis*
8. *Albinism*

#### 820. What is ringworm? What are characteristics of its lesions? How do you diagnose it? Describe the treatment.

**Ans.** Ringworm (*Tinea corporis*) is a fungal skin infection caused by fungi like *Trichophyton*, *Epidermophyton* or *Microsporum*. The characteristic lesions are:

- Single or multiple, small or large, usually circular having a ring of active margin made up of erythematous papules or tiny vesicles (papulo-vesicular scaly active border).
- Lesions resolve centrally and progress peripherally to produce ring-like configuration, hence, the name ringworm.
- The lesion may fluoresce bluish green under Wood's lamp.

**Diagnosis:** It is diagnosed by demonstration of fungi (hyphae and spores) when skin scales, hair or nails are mounted in KOH for several hours and examined under microscope.

#### 821. What are various sites and types of tinea?

**Ans.** These are given in Table 1.175.

#### 822. What is treatment of ringworm?

**Ans.** Following are treatments

1. *General measures*
  - Correction of contributory factor, e.g. diabetes, HIV, hot humid environment, occlusive clothings and footwear

**Table 1.175:** Various sites and types of tinea

Name	Site of involvement
• Tinea corporis	• The whole body
• T. cruris ("Dhobi" itch)	• Thighs and buttocks
• T. capitis	• Scalp
• T. pedis	• Foot
• T. manuum	• Hand
• T. Barbae	• Beard
• T. unguium	• Nail

2. *Topical antifungals*

- Clotrimazole, miconazole, ketoconazole, terbinafin, are used in lotion, cream or powder. Lotions and powders are desirable for intertriginous area and hairy area (scalp)

3. *Systemic antifungals*

- Griseofulvin (micronised) 250 mg twice a day (10 mg/kg/day in children) was till recently the standard treatment for dermatophytosis. The duration of treatment varies from 4 weeks (tinea cruris) to 1-2 years (tinea unguium) depending on the site involved. Now other safe and effective drugs are available as described below
- Ketoconazole is effective in dose of 200 mg once a day, itraconazole is safer and effective (100-200 mg/day) or fluconazole (150 mg/week orally) or terbinafine 250 mg /day is highly effective against all dermatophytes.

Indications for systemic therapy include tinea unguium, tinea pedis, tinea manuum, tinea capitis; widespread or unresponsive or recurring infections of any site in presence of diabetes, immunodeficiency and obesity.

**823. Name the various fungal infection of the skin**

**Ans.** These are divided into superficial and deep infections.

1. *Superficial fungal infection:*

- P. versicolor
- Tinea infection
- Candidiasis

2. *Deep fungal infection*

- Mycotic mycetoma
- Sporotrichosis
- Chromomycosis

**824. Name the opportunistic fungal infection in HIV.**

**Ans.** These are as follows:

- Cryptococcosis
- Mucormycosis
- Aspergillosis
- Candidiasis

**825. What is the treatment of P. versicolor?**

**Ans.** The treatment includes;

- Maintain good personal hygiene
- Topical sodium thiosulphate (25-40% solution) locally is inexpensive therapy used daily for 3 weeks
- Selenium sulphide 2.5% locally at night and wash off in the following morning; 2-3 applications are adequate, weekly shampoo for 3-4 weeks should accompany
- Topical antifungal solutions such as 1% clotrimazole, 2% miconazole, 1% tolnaftate and 2% ketoconazole are effective.
- For recurrence, weekly use of selenium sulphide or zinc pyrithionate shampoo are useful.

### CASE 61: SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

A 20-year female (Fig. 1.61) presented with malar rash, oedema face, alopecia, fever, polyarthritis and fatigue. Examination showed hypertension (BP 180/100 mmHg). There was no positive finding on systemic examination.



**Fig. 1.61:** Systemic lupus erythematosus. Note the butterfly (heliotrophic) rash

#### 826. What is your probable clinical diagnosis?

**Ans.** The malar rash (butter-fly rash) with alopecia, hypertension and polyarthritis in a female patient suggest the diagnosis of systemic lupus erythematosus (SLE).

#### 827. Describe the face of the patient.

**Ans.** The patient has typical lupus face consisting of;

- Classical photosensitive 'butter fly' rash over the nose extending over the malar areas
- Patchy alopecia
- Lupus hairs – short broken hair seen above the forehead
- Oral ulcers seen on opening the mouth.

#### 828. What do you understand by the term SLE?

**Ans.** Systemic lupus erythematosus is a inflammatory disease of unknown aetiology, characterised by inflammation and damage to different tissues and cells by pathogenic autoantibodies and immune complexes.

#### 829. What are skin manifestations of SLE?

**Ans.** The cutaneous manifestations of SLE can be

divided into acute, subacute and chronic (i.e. discoid LE). In addition to 'butter-fly rash', the other lesions are:

- Ill-defined, discrete erythematous papules (papulosquamous form) on the back, chest, shoulders and extensor surfaces of arms and hands. There is associated scaling
- Sometimes annular lesions resembling erythema multiforme may appear as an oral or circular erythematous papules
- Purpura
- Bullous lesion
- Panniculitis
- Digital infarcts
- Livedo reticularis
- Raynaud's phenomenon
- Angioneurotic oedema
- Pigmentation and patchy alopecia.

#### 830. What is discoid lupus?

**Ans.** Discoid lupus is a chronic skin lesion in SLE characterised by:

- Circular lesions with an erythematous rim over the face, scalp or external ears
- Follicular plugging (thick scales occlude the hair follicles). When scales are removed, its underside will show small excrescences that correlate with the openings of hair follicles and is termed a "carpet track appearance". This finding is specific for DLE
- Long-standing lesions develop scarring and atrophy
- Hypopigmentation
- Telangiectasia

**Note:** Only 5 to 10% patients with DLE develop systemic involvement (i.e. turn into SLE). On the other hand, DLE occurs in 20% patients of SLE. DLE is associated with positive antinuclear factor (ANF) and normal complement. Direct immunofluorescence microscopy shows deposits of immunoglobulin and complement at the basement membrane in 90% cases.

#### 831. What are the causes of SLE?

**Ans.** Aetiological factors incriminated in SLE are:

1. Genetic
  - HLA B<sub>8</sub>, DR<sub>3</sub>, DR<sub>2</sub>
  - Inherited complement deficiencies, C<sub>4</sub> null allele



## 2. Environmental

- UV light
- Physical and emotional stress
- Infection
- Female sex hormones
- Drugs, e.g. procainamide, quinidine, hydralazine, methyldopa, isoniazide, chlorpromazine

### 832. What are clinical manifestations of SLE?

**Ans.** They are tabulated (Table 1.176) according to frequency of occurrence.

### 833. What are the criteria for diagnosis of SLE?

**Ans.** Following are the criteria for diagnosis:

1. Malar rash
2. Discoid rash
3. Photosensitivity
4. Oral ulcers
5. Arthritis (nonerosive polyarthritis)
6. Serositis (pleuritis or pericarditis)
7. Renal involvement, e.g.
  - i. Proteinuria  $>0.5$  g/d **or**
  - ii.  $> 3+$  **or**
  - iii. Cellular casts
8. Neurological, e.g.
  - Seizure or psychosis without any other cause
9. Hematological
  - Hemolytic anaemia or leukopenia ( $<4000/\mu\text{l}$ ) **or**
  - Lymphopenia ( $<1500/\mu\text{l}$ ) **or**
  - Thrombocytopenia ( $< 1$  lac/ $\mu\text{l}$ ) in the absence of an offending drug
10. Immunological evidence
  - Positive LE cells **or**
  - Anti-ds DNA or anti-Sm antibodies **or** false positive VDRL.
11. Antinuclear antibodies
  - An abnormal titre of ANAs (positive ANA) in the absence of drugs known to induce it.

**N.B.:** If four of these eleven criteria are met at any time during the course of the disease, a diagnosis of SLE can be made with 98 per cent specificity and 97 per cent sensitivity.

### 834. Name the autoantibodies in SLE.

**Ans.** The autoantibodies in SLE are:

1. Antinuclear antibodies against multiple nuclear

**Table 1.176:** Frequency-wise clinical manifestations of SLE

1. <i>General systemic (95%)</i>
Fatigue, fever, malaise, anorexia, weight loss
II. <i>Musculoskeletal (95%)</i>
• Arthralgia /arthritis
• Myositis/myopathy
III. <i>Cutaneous (80%)</i>
• Malar rash
• Photosensitivity
• Oral ulcers
• Discoid rash
• Alopecia
• Vasculitis
• Panniculitis
IV. <i>Hematological (70%)</i>
• Anaemia, leucopenia, thrombocytopenia
• Lupus anticoagulant (anti-phospholipid syndrome)
• Splenomegaly and lymphadenopathy
V. <i>Neurological (50%)</i>
• Headache, migraine
• Cognitive dysfunction
• Organic brain syndromes (e.g. psychosis, seizures)
• Cranial nerve involvement, hemiplegia
• Transverse myelitis
• Peripheral neuropathy
• Extrapyrarnidal disorders (chorea) and cerebellar dysfunction
VI. <i>Cardiopulmonary (50%)</i>
• Pleurisy
• Pericarditis/ myocarditis
• Endocarditis (Libman-Sachs)
• Pneumonitis
• Pleural effusion
• Interstitial fibrosis/fibrosing alveolitis
• ARDS
• Heart blocks and arrhythmias
VII. <i>Renal (50%)</i>
• Proteinuria, haematuria
• Nephrotic syndrome
• Renal failure
• Urinary tract infection
VIII. <i>Ocular (50%)</i>
• Conjunctivitis /episcleritis
• Retinal vasculitis
• Sicca syndrome
IX. <i>GI tract (30%)</i>
• Nausea, anorexia, diarrhoea
• Abnormal liver enzymes
• Vasculitis with bleeding
• Arterial/ venous thrombosis
X. <i>Foetal loss (30% of pregnancies)</i>

antigens. These are sensitive but not specific autoantibodies

2. Anti-ds DNA is more specific than anti-s DNA
3. Anti-Sm (specific for SLE)
4. Anti-RNP – present in mixed connective tissue disease.
5. Anti-RO (SS-A) is associated with ANA negative lupus,
6. Anti-LA (SS-B) occurs in neonatal lupus, in elderly Sjögren's syndrome
7. Anti-histone, e.g. drug-induced lupus
8. Antiphospholipid, antibodies (e.g. three types are recognised such as lupus anticoagulant, anti-cardiolipin and false positive serology for syphilis)
9. Anti-erythrocytes antibodies
10. Anti-platelet, anti-lymphocyte antibodies
11. Anti-neuronal, e.g. in diffuse CNS lupus
12. Anti-ribosomal P, e.g. in psychosis, CNS lupus.

**835. What is an autoantibody? Which antibody is more sensitive and which one is more specific for SLE?**

**Ans.** Autoantibody means antibody produced against own (self) antigen. Antinuclear antibodies (ANAs) mean antibodies produced against nuclear components of a cell.

Antinuclear antibodies are the best screening test as they are more sensitive. A positive ANA test is not specific for SLE as it is produced by;

- Normal individual (low titre)
- Other autoimmune diseases
- Viral infections
- Chronic inflammatory diseases
- Several drugs induce ANA

Anti-Sm is specific for SLE

**836. What are antiphospholipid antibodies and what is their significance in SLE?**

**Ans.** A syndrome resulting from the production of antiphospholipid antibodies (e.g. lupus anticoagulant, anticardiolipin and false-positive VDRL) is called antiphospholipid syndrome, commonly seen in SLE and other autoimmune disorders.

The presence of these antibodies is associated with;

- Increased coagulopathy (arterial, venous thrombosis)
- Foetal loss

- Thrombocytopenia
- Valvular heart disease

**837. What is antiphospholipid antibody syndrome (APS)? How do you classify them? What are its clinical presentation and treatment?**

**Ans.** The antiphospholipid antibody syndrome (APS) is said to be present if the patient has persistently elevated (twice at least 3 months apart) levels of anti-phospholipid antibody and/or positive lupus anticoagulant test, and the presence of one of the following, i.e. arterial or venous thrombosis, foetal loss, thrombocytopenia.

**Causes of APS**

1. Primary – no definite cause is known.
2. Secondary
  - SLE
  - Drug-induced lupus
  - Infections
  - Malignancy.

**Clinical features of APS**

- Recurrent thromboembolism
- Recurrent foetal loss (2 or more)
- Livedo reticularis
- Nonstroke neurological manifestations
- Valvular heart disease
- Thrombocytopenia
- Catastrophic vascular occlusion

**Classification of APS**

Type I : DVT with pulmonary embolism

Type 2 : Coronary and peripheral artery thrombosis

Type 3 : Cerebrovascular or retinal artery thrombosis

Type 4 : Mixed type

**Treatment**

- Anticoagulants, e.g. heparin including low molecular weight (LMWH)
- Antiplatelets, e.g. aspirin
- Intravenous immunoglobulins (IgG)
- Immunosuppressants and steroids.

**838. How will you investigate a case of SLE?**

**Ans.** The investigations done are:

- Haemoglobin for anaemia. ESR will be raised

- Total leucocyte and differential leucocyte count for leucopenia, lymphopenia and thrombocytopenia
- Urine for hematuria and proteinuria and casts
- Serological tests for syphilis – may be positive
- Autoantibodies detection. The ANA, anti-Sm, anti-DNA and antiphospholipids antibodies are done commonly
- Coombs' test – Direct test may be positive
- Serum complement - low
- Other tests depending on the organ/system involvement.

### 839. What is the treatment of SLE?

**Ans.** Treatment according to severity is as follows;

#### I. *Therapy for mild to moderate disease*

- Bed rest
- NSAIDs and Cox-2 inhibitors
- Antimalarials, e.g. hydroxy-chloroquine, chloroquine for treating lupus rashes and arthritis that do not respond to NSAIDs. Chloroquine 200 mg/day is given. Patient is advised eye check-up after every 6 months.

#### II. *Therapy for SLE with life-threatening manifestations*

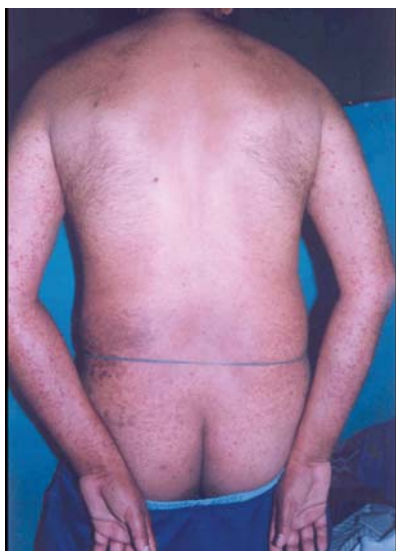
- Topical steroids are used for skin lesions.
- Systemic steroids are used in SLE with life-threatening manifestations such as glomer-

ulonephritis, haemolytic anaemia, myo-pericarditis, CNS involvement and thrombotic thrombocytopenic purpura. The initial dose is 0.5 to 2 mg/kg (average 40-60 mg) orally/ daily for 4-6 weeks, followed by tapered dose 5-10 mg / week to sustain remission.

- Methyl – prednisolone can also be used in the dose of 1 g daily for 3 days followed 0.5 to 1 mg/kg/day of oral prednisolone.
- Lupus nephritis needs renal biopsy for confirmation. Focal renal lesions respond to steroids. However, diffuse proliferative or membranoproliferative forms of nephritis (WHO grades III, IV, V) need cyclophosphamide or azathioprine along with steroids. Dialysis is indicated in renal failure.
- Antiphospholipid syndrome is treated with aspirin and anticoagulation
- Infection is treated with appropriate antibiotics
- *Pregnancy with lupus.* SLE is controlled with the lowest dose of prednisolone for the shortest period. Pregnancy with recurrent foetal loss and antiphospholipid antibodies is treated with aspirin and low molecular heparin.
- SLE with thrombotic thrombocytopenic purpura or haemolytic uremic syndrome is treated by plasmapheresis.

**CASE 62: PURPURA**

A female patient (Fig. 1.62) presented with reddish bluish spots on the upper limbs, trunk and legs. There was no history of itching, fever, joint pains or drug intake. Examination revealed that spots were not elevated from the surface of skin and did not blanch with pressure. They were distributed all over the body.



**Fig. 1.62:** Thrombocytopenic purpura.  
Note the generalised purpuric spots

**840. Describe these spots and what is your clinical diagnosis?**

**Ans.** These spots are haemorrhagic (bluish red), not elevated from the surface and do not blanch with pressure. They are present on the extremities and front and back of the chest.

The diagnosis is nonpalpable purpura.

**841. What is purpura? How does it differ from petechiae and ecchymosis? What is its characteristic feature?**

**Ans.** Purpura is defined as hemorrhagic spots of pin-head size, occurs due to extravasation of blood (RBCs) into the dermis.

Petechiae are smaller haemorrhagic spots ( $\geq 2$  mm) while purpuric spots are larger ( $\geq 3$  mm). The ecchymosis or bruises are still larger purpuric spots/ lesions. Hematoma is a large collection of blood in the skin producing swelling with fluctuation sign positive.

The characteristic feature of purpuric spots is that they do not blanch with pressure by a pin head or glass slide. This feature differentiates it from vasculitis produced by vasodilatation that blanches with pressure. The telangiectasia, mosquito bite marks, spider naevi blanch on pressure, hence, can easily be differentiated.

**842. What are the causes of purpura?**

**Ans.** Purpura may be elevated from the surface (palpable) or may be in line with the surface of the skin (nonpalpable). Primary cutaneous disorders and some systemic diseases produce nonpalpable purpura. *Palpable purpura* is seen in leucocytoclastic vasculitis or allergic vasculitis (Henoch-Schönlein purpura), polyarteritis nodosa and can occur due to infective emboli (e.g. meningococcaemia, disseminated gonococcal infection, Rocky Mountain spotted fever). The causes are tabulated (Table 1.177). Purpuric spots occur either due to platelet defect (qualitative and quantitative) or vessels wall abnormalities, e.g. vasculitis.

**843. What are the causes of non-thrombocytopenic purpura?**

**Ans.** Causes are as follows:

- Infections, e.g. meningococcal, gonococcal, rickettsial and viral
- Allergic purpura (Henoch-Schönlein)
- Hereditary telangiectasia
- Drug – induced
- Senile purpura
- Purpura simplex (Devil's pinches)
- Steroid - induced (Cushing's syndrome)
- Paraproteinaemia
- Vasculitis
- Uraemia

**844. What are causes of thrombocytopenic purpura?**

**Ans.** Thrombocytopenia is caused by one of the three mechanisms:

1. Decreased bone marrow production
2. Increased splenic sequestration
3. Increased /accelerated destruction

Depending on these mechanisms, the causes of thrombocytopenia are summarised in Table 1.178.

**Table 1.177:** Causes of purpura**I. Primary skin disorders**

- a. Non-palpable purpura
  - Trauma
  - Solar purpura
  - Steroid (Cushing's) purpura
  - Capillaritis
  - Livedo vasculitis

**II. Systemic disorders**

- a. Non-palpable
  - i. *Platelet defect*
    - Thrombocytopenia, e.g. idiopathic thrombocytopenic purpura (ITP)
    - Abnormal platelet function
  - ii. *Vascular fragility*
    - Amyloidosis
    - Scurvy
    - Connective tissue disease, e.g. Ehlers-Danlos syndrome
  - iii. *Thrombosis*
    - Disseminated intravascular coagulation (DIC)
    - Cryoglobulinaemia
    - Thrombotic thrombocytopenic purpura
    - Warfarin reaction
  - iv. *Emboli*
    - Cholestrol
    - Fat
  - v. *Immune-complex*
    - Gardner-Diamond syndrome
    - Waldenstrom's hypergammaglobulinaemic purpura
- b. *Palpable*
  - i. *Vasculitis*
    - Allergic purpura (Henoch – Schönlein)
    - PAN (polyarteritis nodosa)
  - ii. *Infectious emboli*
    - Meningococcaemia
    - Disseminated gonococcal infection
    - Rocky Mountain spotted fever
    - Ecthyma gangrenosum

**845. What are clinical characteristic of ITP?**

**Ans.** The three clinical characteristics are:

1. Bleeding is the characteristic feature of ITP which occurs at the following sites;
  - Skin, e.g. petechiae, purpura, ecchymosis
  - Mucous membrane and gum bleeding
  - Nasal bleeding (epistaxis)
  - Genitourinary tract bleeding (haematuria, menorrhagia)
  - Intracranial and intra-abdominal bleeding

**Table 1.178:** Causes of thrombocytopenia**I. Decreased bone marrow production**

- Aplasia/hypoplasia of marrow
- Fanconi syndrome
- Myelophthisic process (malignant infiltration of marrow)
- Deficiency states, e.g. folic acid, vit. B<sub>12</sub>
- Paroxysmal nocturnal haemoglobinuria
- Drugs / physical
- Myelofibrosis

**II. Increased splenic sequestration**

- Infective
- Congestive
- Neoplastic

**III. Increased/Accelerated destruction of platelets**

- A. *Immune*
  - Idiopathic (immune) thrombocytopenic purpura (ITP)
  - SLE
  - Lymphoreticular disorders
  - Hypothyroidism
  - Drugs
- B. *Non-immune*
  - Thrombotic thrombocytopenic purpura
  - Disseminated intravascular coagulation (consumptive coagulopathy)
  - Valvular disorders (microangiopathic)

2. Reduced platelet count

3. Hypercellular marrow with megakaryocytosis.

**846. Name the drugs that cause thrombocytopenic purpura.**

**Ans.** The drugs either suppress platelet production in marrow or cause accelerated platelet destruction. The causes are;

**I. Drugs causing suppression of platelets production**

- Myelosuppressive drugs, e.g. cytosine arabinoside, daunorubicin, cyclophosphamide, busulfan, methotrexate, 6-MP, Vinca alkaloids
- Thiazide diuretics
- Ethanol (binge drinker)
- Oestrogen.

**II. Drugs producing immunological destruction of platelets**

- Antibiotics, e.g. sulphonamide, tetracyclines, novobiocin, PAS, rifampicin, chloramphenicol
- Cinchona alkaloids, e.g. quinine, quinidine
- Sedatives, hypnotic, and anticonvulsants (carbamazepine)



- Digoxin
- Alpha - methyl dopa
- Anti – inflammatory, e.g. aspirin, phenylbutazone
- Chloroquine, gold salts, arsenicals
- Insecticides

#### 847. What are causes of splenomegaly with purpura?

**Ans.** Following are the causes:

1. Lymphoreticular malignancy, e.g. leukaemia and lymphoma, acute blastic crisis of CML and CLL
2. Infections, e.g. subacute infective endocarditis, septicaemia
3. Connective tissue disorders, e.g. SLE
4. Myelofibrosis
5. *Hypersplenism*: Though hypersplenism means hyperfunction of the spleen. The term has nothing to do with the size, but hypersplenism is usually associated with splenomegaly. The causes are;
  - Portal hypertension
  - Myeloproliferative disease
  - Lymphoma

#### 848. What is Henoch–Schnölein purpura (Anaphylactoid purpura)?

**Ans.** It is self-limiting type of vasculitis, occurs in children and young adults, characterised by purpuric spots or urticarial rash on the extensor surfaces of the arms and legs, polyarthralgia or arthritis, abdominal colic and haematuria (focal glomerulonephritis). The syndrome follows an episode of URI or streptococcal pharyngitis. All the coagulation tests are normal despite purpura. Bleeding time is normal.

#### 849. How will you investigate a case with purpura?

**Ans.** The investigations are as follows:

- Haemoglobin – may be low
- Urine for haematuria, proteinuria
- Platelet count – low in thrombocytopenic purpura, normal in non-thrombocytopenic purpura
- Bleeding time is prolonged. Clotting time is normal.
- PTTK and PT (prothrombin time) are normal

- Antiplatelets antibodies. They are present in immune thrombocytopenic purpura
- Serological tests for hepatitis, cytomegalovirus, Epstein- Barr virus and HIV
- Bone marrow examination. It should be done when platelet count is  $>50,000/\mu\text{l}$  and there is no bleeding
- Antinuclear antibodies (ANAs) for SLE
- USG for spleen enlargement
- Radio-labelled platelets and their destruction in the spleen will confirm hypersplenism.

#### 850. What is treatment of ITP?

**Ans.** This is as follows:

- Specific therapy is not necessary unless platelet count is  $<20,000/\mu\text{l}$ . Analgesic (codeine and paracetamol) may be used for pain or fever
- Corticosteroids are used to control bleeding in acute ITP. Oral prednisolone is given in dose of 40-60 mg/day for few weeks followed by tapering of the dose to maintenance dose of 5-10 mg/day
- IV immunoglobulin (IVIG) is reserved for patients with severe thrombocytopenia and clinical bleeding who fail to respond to steroids and other measures
- Blood transfusions/ platelets transfusion is given to raise the platelet count is severe thrombocytopenia.
- *Splenectomy*. It is indicated in patients with ITP who are resistant to other measures
- *Immunosuppressive therapy*. Patients who remain thrombocytopenic after steroid therapy or splenectomy or who relapse within months to years after initial therapy are candidates for immunosuppression with azathioprine, cyclophosphamide or vincristine/vinblastine.

#### 851. How do you diagnose asplenia or hyposplenia?

**Ans.** The diagnostic signs are:

1. Presence of Howell–Jolly bodies, Heinz bodies and basophilic stippling in RBCs. There is marked anisocytosis and poikilocytosis
2. USG will show absence of spleen
3. Radionuclide scan for spleen will confirm its absence.

**852. What are the risks of splenectomy?**

**Ans.** The risks are:

1. Increased susceptibility to bacterial infection by capsular organisms, e.g. *S. pneumoniae*, *H. influenzae* and some *gram-negative organisms*. Immunisation against these may be done before splenectomy.
2. There is increased susceptibility to parasitic disease, e.g. babesiosis in certain endemic areas.

The vaccination schedule before and after splenectomy has already been discussed in case discussion on splenomegaly.

**853. What is Dengue Haemorrhagic Fever? What is Hess capillary test?**

**Ans.** Dengue is a mosquito-borne (*Aedes aegypti*) viral infection caused by one of the 4 types of *flavi viruses* (dengue ito 4), occurs in epidemics, and is characterised by febrile illness (classic dengue), bleeding manifestations (dengue haemorrhagic fever) and shock (dengue shock syndrome).

Dengue haemorrhagic fever is characterised by all manifestations of classic dengue fever, thrombocytopenia (platelet count <1 lac), vascular instability and increased permeability and local haemorrhage (spontaneous petechiae and/or purpura) with positive tourniquet test

called *Hess capillary test*. The haemorrhage in dengue is due to combined effect of vascular damage and thrombocytopenia.

**Hess capillary test (Tourniquet test)**

It is positive in dengue fever and severe thrombocytopenia (ITP). It indicates vascular instability.

It is performed by blood pressure cuff wrapped in upper arm and BP is raised and maintained between systolic or diastolic (usually around 100 mmHg) for 5 minutes. The haemorrhagic spots are counted in a circle marked on the mid-forearm with a diameter of one inch. The haemorrhagic spots more than 10 are abnormal, indicate positive test.

**854. What is critical platelet count?**

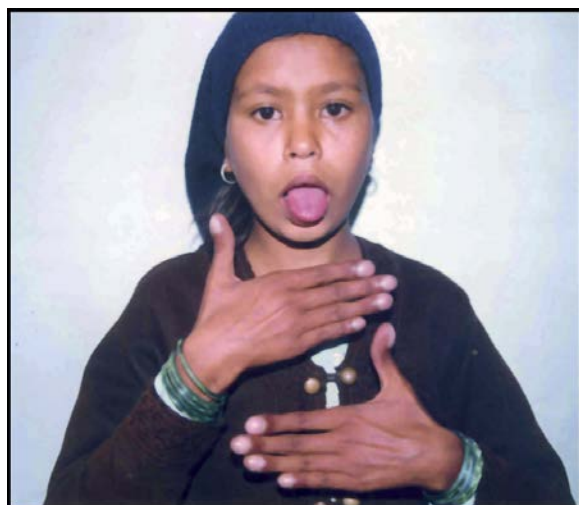
**Ans.** Critical platelet count means the lowest platelet count at which spontaneous bleeding into the skin, brain or internal organs may occur and may be fatal. The critical count is <20,000/ul. The count between 20,000/ul and 50,000/ul leads to bleeding only after minor trauma or stress.

**855. What is difference between bleeding and clotting disorder?**

**Ans.** Read Clinical Methods in Medicine Vol. I.

### CASE 63: CYANOTIC CONGENITAL HEART DISEASE

A 14-year female presented with cyanotic spells (bluishness during exertion), syncope and tachypnoea. On symptomatic enquiry, it was found that she had bluishness of tongue and nails since infancy and childhood which increased during crying or on waking up from sleep. The parents admitted that child used to sit in squatting position after playing. The examination revealed cyanosis, clubbing (Fig. 1.63) and an ejection systolic murmur in 2nd left intercostal space with loud single second heart sound.



**Fig. 1.63:** Congenital cyanotic heart disease. A young female with Fallot's tetralogy. Note the drum-stick clubbing and central cyanosis

#### 856. What is the clinical provisional diagnosis?

**Ans.** The patient has cyanotic congenital heart disease—Fallot's tetralogy.

#### 857. What are the components of Fallot's tetralogy, triology and pentalogy?

**Ans.** Table 1.179 describes all the components of Fallot's.

#### 858. What is the cause of cyanosis in Fallot's tetralogy?

**Ans.** This is due to mixing of the unoxygenated blood from right ventricle to left ventricle through VSD as the shunt between two ventricles is either bidirectional (blood flows from either ventricles depending on the pressure) or from right to left and the over-riden aorta gets mixed blood from both the ventricles leading to cyanosis.

Note: Right to left shunt produces cyanosis; left to right shunt does not.

#### 859. Name few common cyanotic and acyanotic congenital heart disease.

**Ans.** These are as follows:

##### Cyanotic congenital heart disease

- Fallot's tetralogy
- Transposition of great vessels
- Total anomalous pulmonary venous drainage
- Single ventricle
- Truncus arteriosus
- Tricuspid atresia
- Ebstein's anomaly (some cases are cyanotic)
- Eisenmenger's complex and syndrome.

Acyanotic congenital heart disease. These are either with left to right shunt or with outflow tract obstruction.

##### 1. Left to right shunt

- ASD, VSD, PDA
- Endocardial cushion defects
- Rupture of sinus of valsalva
- Coronary arteriovenous fistula

##### II. Obstructive lesions

- Coarctation of aorta
- Congenital aortic stenosis
- Congenital pulmonary stenosis

**Table 1.179:** Components of Fallot's tetralogy, triology and pentalogy

Fallot's tetralogy	Fallot's triology	Fallot's pentalogy
<ul style="list-style-type: none"> <li>• VSD</li> <li>• Pulmonary stenosis</li> <li>• Right ventricular hypertrophy</li> <li>• Over-riding of aorta</li> </ul>	<ul style="list-style-type: none"> <li>• VSD</li> <li>• ASD</li> <li>• Pulmonary stenosis</li> </ul>	<ul style="list-style-type: none"> <li>• ASD is added to Fallot's tetralogy to make it pentalogy</li> </ul>

**860. What is the cause of ejection systolic murmur in this case?**

**Ans.** In Fallot's tetralogy, there is pulmonary stenosis which produces an ejection systolic murmur and single second heart sound. The pulmonary stenosis in Fallot's tetralogy may be infundibular (common) or valvular (uncommon).

**861. Why VSD in Fallot's does not produce murmur?**

**Ans.** Murmur is produced due to presence of a flow gradient across a congenital defect or a valve. In Fallot's, the shunt at VSD level is more or less balanced without much flow gradient across the defect, hence, murmur is not produced.

**862. What is Eisenmenger's complex and Eisenmenger's syndrome?**

**Ans.** In VSD, there is usually left to right shunt.

*Eisenmenger's complex* means a VSD with reversal of shunt (right → left).

*Eisenmenger's syndrome* means reversal of any left to right shunt (e.g. ASD, PDA) except VSD.

**863. How does squatting position helps in Fallot's tetralogy?**

**Ans.** Squatting is the posture adopted by children with Fallot's tetralogy in which child sits with flexed hips and knees. It helps to reduce venous return of desaturated blood and an increase in peripheral vascular resistance, thus, reduces right to left shunting and improves cerebral oxygenation. This posture reduces cyanotic spells.

**864. What are genetic and environmental factors implicated in congenital heart diseases?**

The various factors associated with congenital heart disease are tabulated (Table 1.180).

**865. What is ASD? What are its type and physical signs?**

**Ans.** Atrial septal defect (ASD) is a common cardiac anomaly manifesting in adults more commonly in women. In this condition, there is defect in atrial septum

**Table 1.180:** Genetic and environmental factors and associated congenital heart disease

I. Genetic factors	Associated cardiac defects
A. Chromosomal defects	Associated Cardiac defects
• Trisomy 21 (Down's syndrome)	VSD, ASD, PDA, Fallot's tetralogy
• Trisomy 13 (Patau's syndrome)	VSD, ASD, PDA
• Trisomy 18 (Edward's syndrome)	VSD, PDA
• Turner's syndrome (45X0)	Coarctation of aorta
• Cri-du-chat (Short arm deletion -5)	VSD
• XXXY and XXXXX	PDA
B. Single gene defect	
• Ellis-Van Creveld (R)	ASD, single atrium
• Carpenter's syndrome (R)	PDA, ASD
• Holt-Oram (D)	ASD, VSD
• Noonan syndrome (D)	Pulmonary stenosis, aortic stenosis, ASD
II. Environmental factors	
• Maternal rubella	PDA, peripheral pulmonary stenosis
• Maternal alcohol abuse	Septal defects (ASD, VSD)
• Cocksackie virus	PDA, VSD
• Thalidomide	ASD, VSD, truncus arteriosus
• Maternal SLE	Congenital complete heart block
• Maternal DM	VSD, transposition of great vessels, coarctation of aorta
Abbrev. ASD – atrial septal defect VSD – ventricular septal defect PDA – patent ductus arteriosus	

**Table 1.181:** Classification of ASD

Types	Defects
<i>Ostium secundum</i> (commonest)	At the level of fossa ovalis
<i>Sinus venosus</i>	Posterior to foramen ovale
<i>Coronary sinus</i>	Inferior and anterior to foramen ovale
<i>Ostium primum</i> (rare)	Anterior and inferior to foramen ovale and cleft mitral and tricuspid valves

leading to shunting of blood from left atrium to right atrium (LA→RA). It is acyanotic congenital heart disease.

Types and defects are given in Table 1.181.

Physical signs in ASD are;

1. **Sternal impulse (heave).** There is right ventricular impulse or heave
2. **Sounds.** Ist sound is loud. The second heart sound is loud, fixed and widely split.
3. **Murmurs**
  - A grade 2 or 3 pulmonary ejection or midsystolic murmur best heard at 2nd or 3rd left interspace
  - A short diastolic flow murmur in tricuspid area (e.g. at lower left sternal border).

Both these murmurs are flow murmurs. There is no murmur due to left to right shunt across the defect because of low pressure gradient between two atria.

### 866. What are characteristics of VSD?

**Ans.** Ventricular septal defect is the commonest congenital heart disease (25-30% of all congenital heart diseases) in which there is abnormal communication between left and right ventricles at ventricular septal level leading to shunting of blood from left to right (L → R) hence, it is acyanotic heart disease.

#### Types of defect

1. Perimembranous (membranous part of septum involved)
2. Muscular (muscular part involved)

The haemodynamics in VSD include shunting of oxygenated blood from left to right ventricle causing overloading of right ventricle, consequently the pulmonary artery and lungs (pulmonary plethora).

The physical signs include;

**Apex beat:** hyperkinetic, ill-sustained

**Sternal lift/heave** (left sternal heave)

**Thrill** –Palpable systolic thrill at left sternal edge/ or across the sternum

#### Sounds

- First and second heart sounds are masked by pansystolic murmur in the left parasternal region as well as across the sternum
- The second heart sound may be normal or loud with wide or normal splitting or narrow splitting if pulmonary arterial hypertension develops
- A third heart sound (S<sub>3</sub>) may be heard.

#### Murmurs

- A pansystolic or holosystolic murmur heard across the sternum. The pansystolic murmur is replaced by an ejection systolic or short systolic murmur in a large VSD due to sudden equalisation of pressures and early loss of gradient across the defect.
- With large shunts, an apical mid-diastolic flow murmur may also be heard.

### 867. What are the causes of pansystolic murmur?

**Ans.** Causes are as follows:

- VSD
- Mitral regurgitation/mitral valve prolapse
- Tricuspid regurgitation
- Rupture of chordae tendinae
- Rupture of interventricular septum
- Dilated cardiomyopathy
- Left heart failure due to dilatation of mitral valve ring.

### 868. What is maladie de roger?

**Ans.** It is asymptomatic small haemodynamically insignificant VSD where a pansystolic murmur is the only evidence.

### 869. What is PDA? What are its characteristics?

**Ans.** The ductus arteriosus is normally present in the foetus and allows the right ventricular output to enter the descending aorta as the lungs are non-functioning and the pulmonary circulation is not essential in foetal life.

It closes within 24-48 hours after birth as the lungs expands and pulmonary circulation established. Premature babies commonly have PDA (patent ductus



arteriosus) which closes spontaneously when the baby reaches the full term.

PDA means persistence of ductus arteriosus after birth leading to shunting of blood from aorta to pulmonary artery (L→R shunt).

This is the commonest lesion in babies with rubella syndrome, premature baby and babies born at high altitude. Haemodynamics include a continuous flow of blood from the aorta to pulmonary artery during systole leading to overloading of the lungs (pulmonary plethora) and left atrium and left ventricle.

### Physical Signs

**Signs of hyperdynamic circulation**, e.g. bounding peripheral pulses, tachycardia, pulsations in suprasternal notch and carotid pulsations, wide pulse pressure.

**Apex beat** – hyperkinetic /forceful but ill sustained

**Thrill** – A systolic or continuous thrill may be palpable rarely at the 2nd left interspace.

### Sounds

- The first sound is loud
- The second sound is loud with narrow split in small shunts but paradoxically split in large shunt.
- A third heart sound at the apex is common

### Murmurs

- A continuous ‘machinery’ murmur (Gibson’s murmur) is heard at 2nd left intercostal space below clavicle
- A mid-diastolic murmur (flow murmur) at apex due to left to right shunt.

### 870. What is a continuous murmur? What are its causes?

**Ans.** A continuous murmur is defined as a murmur which starts with the first heart sound ( $S_1$ ), continues throughout the systole and peaks at the second heart sound ( $S_2$ ) and spills into diastole after the sound (waning character).

### Causes

- PDA
- Aortopulmonary window
- Rupture of sinus of valsalva into right atrium or ventricle

- Coronary arteriovenous fistulae
- Pulmonary arteriovenous fistula
- Heard over the collateral vessels
- Peripheral pulmonary artery stenosis

### 871. What are radiological characteristics of left to right shunts? (Read the radiological section 4)

**Ans.** Chest X-ray (PA view) shows;

- Prominent heart shadow or cardiomegaly with left ventricular configuration
- The pulmonary conus is prominent
- Pulmonary plethora (increased bronchovascular marking from hilum to periphery) present
- The aortic knuckle is also prominent

### 872. What are clinical hallmarks of a large left to right shunt?

**Ans.** The clinical hallmarks are due to hyperkinetic circulation with systemic overloading. The various signs are;

- Bounding pulses, may be *water-hammer*
- Prominent carotid and suprasternal pulsations
- Palpable parasternal heave
- Hyperkinetic apical impulse
- Loud sounds (1st and 2nd) and presence of 3rd heart sound
- Flow murmurs across the valves usually mid-diastolic either at mitral or tricuspid valve or an ejection systolic murmur across the semilunar valves.

### 873. What is the site of infective endocarditis in left to right shunt?

**Ans.** The infective endocarditis develops where the jet of blood flow strikes the ventricle or the vessel, i.e. right ventricular wall in VSD and wall of pulmonary vessel in PDA. The endocarditis in ASD is rare due to slow flow of blood.

### 874. Which congenital heart diseases can cause atrial fibrillation?

**Ans.** The disease are:

- ASD
- Ebstein anomaly

### CASE 64: SUPERIOR MEDIASTINAL COMPRESSION

A patient (Fig. 1.64) presented with cough, dyspnoea, fever, chest discomfort, puffiness of face, hoarseness of voice. The examination showed suffused face, cyanosis, prominent engorged neck veins with absent pulsations and hoarseness of voice. There was enlargement of cervical lymph nodes. Heart was essentially normal.



**Fig. 1.64:** Superior mediastinal compression due to a mass in the mediastinum. Note the prominent neck veins and veins over the upper part of chest above the nipple line

**875. What do the symptoms and signs indicate?**

**Ans.** The symptoms and signs indicate superior mediastinal compression.

**876. What is superior mediastinal compression?**

**Ans.** Superior mediastinum is an area bounded above by thoracic inlet, below by the upper part of heart and vessels, anteriorly by sternum and posteriorly by spines. It contains, lymph nodes, thymus, aortic arch, trachea, superior vena cava, oesophagus and connective tissue.

Compression in this area due to any cause results in pressure on these structures including superior vena cava leading to clinical picture of superior mediastinal syndrome or superior vena cava syndrome.

**877. What are the causes of superior mediastinal compression?**

**Ans.** They are summarised in Table 1.182.

**Table 1.182:** Causes of superior mediastinal compression

<b>I. Enlarged lymph nodes</b>
• Tuberculosis
• Lymphoma
• Sarcoidosis
• Leukaemia
<b>II. Thymus</b>
• Thymic hyperplasia or thymoma
<b>III. Thyroid</b>
• Retrosternal goitre
<b>IV. Aorta</b>
• Aortic aneurysm
<b>V. Oesophageal lesions</b>
• Carcinoma
<b>VI. Tumours</b>
• Vascular
• Teratoma

**878. What are symptoms and signs of superior mediastinal compression or superior vena cava compression (SVC)?**

**Ans.** These are enlisted in Table 1.183.

**879. How the neck veins look like in superior mediastinal compression (SMC)?**

**Ans.**

- The neck veins are engorged, dilated and may be tortuous
- Venous pulsations are absent
- Hepatojugular reflux is positive.
- There is no inspiratory collapse of the veins due to obstruction between veins and right atrium.

**880. What conditions will you keep in mind in such a case?**

**Ans.** All the conditions that produce puffiness of face will come into differential diagnosis.

- Pericardial effusion/constrictive pericarditis
- Cardiomyopathy (restrictive, dilated)
- CHF
- Cor pulmonale
- Valvular heart diseases

**881. How will you investigate such a case?**

**Ans.** The investigations are as follows:

1. TLC, DLC for tuberculosis, lymphoma and leukaemia
2. Chest X-ray (PA view) to identify the anatomical site of tumour and its effects, i.e.:
  - Mediastinal widening

**Table 1.183:** Clinical features of superior mediastinal compression

Structure compressed	Symptoms and signs
i. <b>Trachea</b>	Respiratory distress, stridor, cough
ii. <b>Oesophagus</b>	Dysphagia (solids and liquids)
iii. <b>Bronchus</b>	It is usually not involved except in bronchogenic carcinoma, producing collapse of the lung
iv. <b>Nerves</b>	
– Recurrent laryngeal	Hoarseness of voice, bovine cough, stridor
– Phrenic	Breathlessness and hiccough
– Cervical sympathetic	Horner's syndrome
v. <b>Vessels</b>	
– Superior vena cava	Suffused and puffy face, visual disturbances, headache, alteration in consciousness, prominent engorged neck veins without pulsations, chemosis
– Azygos vein	Right sided pleural effusion
– Lymphatics	Non-pitting oedema of upper thorax, chylothorax

- Collapse or atelectasis
  - Malignancy lung
  - Pleural effusion
  - Raised hemidiaphragm (phrenic nerve palsy)
  - Rarely pericardial effusion
3. Sputum for AFB and malignant cells
  4. FNAC or excision biopsy of palpable lymph node (scalene node, Virchow's gland or any other node)
  5. Pleural fluid aspiration and pleural biopsy
  6. Barium swallow for oesophageal compression
  7. CT scan of thorax or lung scan or thyroid scan.

### 882. What is inferior vena caval compression (IVC) syndrome?

**Ans.** Compression or obstruction of inferior vena cava occurs due to ascites, tumours of the abdomen or pelvis, pregnant uterus, thrombosis extending from pelvic veins, membranous obstruction, oral contraceptives use and myeloproliferative disorders. The clinical picture resulting from IVC obstruction include:

- Oedema (pitting) of legs with dilated veins over the legs
- Collateral veins are seen over the abdomen, flanks and back
- Direction of blood flow in abdominal veins is "below upwards"
- Ascites
- Chronic venous ulcer and staining of ankles in chronic cases
- Signs of portal hypertension (post-hepatic) if venous obstruction is above the joining of hepatic veins

### 883. What is pneumomediastinum?

**Ans.** Pneumomediastinum means collection of air into the mediastinal space.

The causes are;

1. *Alveolar rupture with dissection of air into the mediastinum*
  - Acute severe asthma
  - Pneumocystis carinii pneumonia
2. *Perforation of oesophagus, trachea or bronchi*
  - Aspiration of a foreign body
  - Severe straining during coughing or vomiting in children. Weight lifting and glass blowing may also predispose to it.
  - Manipulation (iatrogenic)
  - Blunt trauma to the chest
3. *Dissection of air from the neck or abdomen into the mediastinum*
  - Blunt trauma to neck
  - Difficult parturition
  - Perforation of a hollow viscus and collection of air into retroperitoneal space and then dissection into mediastinum.

### Clinical Signs

- Subcutaneous emphysema in suprasternal notch with pain and dyspnoea
- *Hamman's mediastinal sign* – a crunching sound synchronous with heart beat is best heard in left lateral decubitus position on compression of mediastinum with palm of the hand.
- Chest X-ray shows air column parallel to heart and aorta, best seen in lateral film.

**CASE 65: PERICARDITIS WITH EFFUSION**

The patient presented with chest pain, dyspnoea, distension of the abdomen and oedema feet. There was past history of fever without cough and haemoptysis. Examination of CVS revealed pericardial rub with enlargement of cardiac area of dullness and feeble heart sounds. The neck veins were engorged and JVP was raised with prominent X-descent. Kussmaul's sign was negative (Fig. 1.65).



**Fig. 1.65:** Pericarditis with effusion. The diagnostic pericardiocentesis is being done

**884. What is the clinical provisional diagnosis?**

**Ans.** Pericarditis with pericardial effusion.

**885. How do you classify pericarditis?**

**Ans.** Depending on the duration, pericarditis is classified as;

**1. Acute pericarditis (< 6 weeks)**

- Fibrinous
- Serous or sanguineous

**2. Subacute pericarditis (6 weeks to 6 months)**

- Effusive – constrictive
- Constrictive

**3. Chronic pericarditis (> 6 months)**

- Constrictive
- Effusive (with pericardial effusion)
- Adhesive (non-constrictive).

**886. What are the causes of pericarditis?**

**Ans.** They are tabulated (Table 1.184).

**Table 1.184:** Causes of pericarditis

**A. Idiopathic or nonspecific**

**B. Infections**

- *Viral*, e.g. coxsackie virus A and B, echovirus, mumps, adenovirus, hepatitis, HIV
- *Bacterial*, e.g. tubercular, pyogenic organisms (pneumococci, staphylococci, streptococci and Neisseria)
- *Fungal*, e.g. histoplasmosis, candida, blastomycosis, (coccidioidomycosis)
- *Parasitic*, e.g. echinococcus, amoebiasis and filariasis

**C. Non-infectious**

- i. Postmyocardial infarction
- ii. Metabolic, e.g. uraemia, hypercholesterolemia
- iii. Endocrinal, e.g. myxoedema
- iv. Neoplastic, e.g. primary (benign or malignant) and secondary (metastases from lung and breast cancer)
- v. Traumatic, e.g. penetrating and non-penetrating injury
- vi. Aortic dissection (blood leakage into pericardium)
- vii. Post-radiation
- viii. Familial mediterranean fever (FMF).

**D. Hypersensitivity or autoimmune**

- Rheumatic fever
- Collagen vascular disorders, e.g. SLE, rheumatoid arthritis, scleroderma, acute rheumatic fever
- Drug-induced, e.g. procainamide, hydralazine, isoniazide, phenytoin, doxorubicin, methyl dopa
- Post-cardiac injury, e.g. postmyocardial infarction (Dressler's syndrome), post-pericardiotomy

**887. What is pericardial rub? What does it indicate? What are its characteristics? How does it differ from pleuropericardial rub?**

**Ans.** It is an adventitious sound produced by rubbing of visceral and parietal pericardium, hence, has a rubbing or scratching quality. It may have presystolic, systolic or early diastolic components which means rub may be heard in a part of systole or throughout systole or in early diastole.

It explains the pain due to pericarditis. The pericardium being pain-sensitive structure leads to pain during rubbing or scratching of its layers against each other.

*Its characteristics are:*

- High pitched, scratching and grating sound or to and fro leathery sound
- It is heard over precordium at the left lower sternal border on pressure with diaphragm of the stethoscope



- It is best heard during expiration with patient in the sitting position and leaning forward
- It is inconsistent, may appear intermittently
- It may disappear after few hours and may appear next day
- It may be heard during a part of systole or throughout systole or in early diastole.

It does not have any relation to respiration, hence, differs from pleuropericardial rub (Read the Clinical Methods in Medicine Vol. I).

Its differentiation from continuous murmur are given in Table 1.185.

### 888. What are clinical characteristics of acute pericarditis?

**Ans.** Pain, a pericardial rub and characteristic ECG changes (ST segment elevation with concavity upwards in more than two or three standard leads and  $V_2$ - $V_6$ ) are clinical hallmarks (a triad) of acute pericarditis.

### 889. What are ECG changes in acute pericarditis?

**Ans.** Read Practical Electrocardiography by Prof. S.N. Chugh

### 890. When does pericardial rub disappear in pericarditis?

**Ans.** As pericarditis indicates friction between two layers of the pericardium, the rub persists as long as friction persists in pericarditis, may disappear with appearance of massive pericardial effusion or development of chronic calcific pericarditis. It is possible to hear a pericardial rub in effusive pericarditis (pericarditis with minimal effusion).

### 891. What are characteristics of pericardial effusion?

**Ans.** The pericardial cavity contains about 50 ml or less of pericardial fluid, which may be detected on echocardiography. The pericardial effusion means collection of fluid (exudate, transudate, pus or blood) in the pericardial cavity more than normal but the signs will appear only if it is more than 200 ml.

*The symptoms are:*

- Pain, central in origin having all characteristics described in pericarditis
- Dyspnoea due to compression of lung and bronchi
- Dry hacking cough, hoarseness of voice and dysphagia due to compression of trachea, recurrent laryngeal nerve and oesophagus respectively.

The signs of pericardial effusion are given in Table 1.186.

### 892. What is cardiac tamponade? What are its salient features?

**Ans.** It is defined as acute massive collection of fluid leading to an impaired filling of ventricles due to rising intrapericardial pressure. There is decrease in stroke volume due to impaired cardiac contractions.

*Note.* Tamponade is associated with acute or rapid collection of fluid; whereas large pericardial effusion which has developed slowly may not result in tamponade.

*Its salient features are;*

- Breathlessness, cyanosis and patient assumes knee-chest position
- Tachycardia
- Pulsus paradoxus, low volume pulse
- Raised JVP. Neck veins full and pulsations present

**Table 1.185:** Differences between a continuous murmur and pericardial rub

<i>Pericardial rub</i>	<i>Continuous murmur</i>
<ul style="list-style-type: none"> <li>• Rubbing or scratching sound</li> <li>• Heard either in a part of systole or diastole</li> <li>• Best heard in sitting position during expiration with patient sitting up and leaning forward</li> <li>• Associated with pain</li> <li>• Inconsistent and intermittent in character, i.e. may appear and then disappear for few hours</li> </ul>	<ul style="list-style-type: none"> <li>Soft musical or machinery sound</li> <li>Heard both in systole and diastole</li> <li>Heard in all positions</li> <li>Not associated with pain</li> <li>Consistent in character</li> </ul>



**Table 1.186:** Signs of pericardial effusion

<b>General physical signs</b>	
•	<i>Pulsus paradoxus</i>
•	Low pulse pressure
•	Cyanosis may or may not be present
•	Neck veins are distended and Kussmaul's sign is absent
•	Pitting oedema feet
<b>Systemic examination</b>	
<i>Inspection</i>	
•	Precordium may be bulging including xiphisternum
•	Apex is not visible
•	No other pulsations are visible
<i>Palpation</i>	
•	Apex beat is either feeble or not palpable
•	A pericardial rub may be palpable
•	No other pulsations palpable
•	Palpable tender liver (tender hepatomegaly)
<i>Percussion</i>	
•	Increase in area of cardiac dullness. Shifting cardiac dullness may be present (area of cardiac dullness decreases on sitting)
•	There is an area of dullness, on right side of sternum in 5th intercostal space (Rotch's sign)
•	An area of dullness in the left interscapular region with bronchial breathing and aegophony (Edward's sign). This is due to compression of base of the lung
<i>Auscultation</i>	
•	Heart sounds are muffled
•	A pericardial rub may be heard
<b>Other signs</b>	
•	Tender hepatomegaly
•	Ascites

- Fall in BP with low pulse pressure. There may be hypotension or shock
- Kussmaul's sign (paradoxical rise in JVP during inspiration) is absent
- Muffled heart sounds

Rising venous pressure, fall in arterial pressure and quiet heart constitute a triad of cardiac tamponade

*Treatment* (Read Medical Emergencies by Prof. S.N. Chugh)

It is two fold;

- Pericardiocentesis (removal of pericardial fluid)
- Treatment of the underlying cause.

### 893. What is chronic constrictive pericarditis?

**Ans.** The disorder results following healing of acute fibrinous or serofibrinous pericarditis or a chronic pericardial effusion leading to obliteration of the pericardial sac with granulation tissue and ultimately a firm scar encasing the heart is formed. Like pericardial effusion, it also interferes with filling of the ventricles.

The causes of constrictive pericarditis are:

#### A. Infectious

- Tubercular pericarditis (commonest)
- Pyogenic pericarditis
- Acute viral pericarditis
- Fungal (histoplasmosis) pericarditis

#### B. Non-infectious

- Neoplasm
- Post-radiation
- Post-traumatic
- Following cardiac surgery
- Collagen vascular disorder, e.g. SLE, rheumatoid arthritis
- Chronic renal failure treated by haemodialysis

The clinical features resemble with that of cardiac tamponade, right heart failure (Table 1.187).

**Table 1.187:** Distinction between chronic constrictive pericarditis, pericardial effusion and right ventricular failure

<i>Features</i>	<i>Pericardial effusion</i>	<i>Constrictive pericarditis</i>	<i>Right heart failure</i>
<b>A. Clinical</b>			
Pulsus paradoxus	Common	Absent	Absent or rare
Jugular veins, e.g.			
Prominent y descent	Absent	Present	Rare
Prominent x descent	Present	Absent	Rare
Kussmaul's sign	Absent	Present	Absent
Third heart sound (S <sub>3</sub> )	Absent	Absent	May be present
Pericardial knock (rub)	Absent	Often present	Absent
<b>B. ECG</b>			
Low voltage graph	Present	May be present	Absent
Electrical alternans	Present	Absent	Absent
<b>C. Echocardiography</b>			
Thickened pericardium	Absent	Present	Absent
Pericardial calcification	Absent	Often present	Absent
Pericardial effusion	Present	Absent	Absent
RV size	Usually small	Normal	Enlarged
Right atrial collapse	Present	Absent	Absent
Increased early filling with increased mitral flow velocity	Absent	Present	May be present
Exaggerated respiratory variation in flow velocity	Present	Present	Absent
<b>D. CT and MRI</b>			
Thickened/calcified pericardium	Absent	Present	Absent
<b>E. Cardiac catheterisation</b>			
Equalisation of diastolic ventricular pressure pulses-square root sign	Present	Present	Absent or present

**CASE 66: POLYARTHRITIS**

A young female presented with history of long duration (few years) of joint pains involving the small joints of both the hands followed by deformities (Fig. 1.66).



**Fig. 1.66:** Polyarthritis. A young female patient with bilateral symmetrical deforming polyarthritis-rheumatoid arthritis. Note the various deformities

**894. What is probable diagnosis and why?**

**Ans.** The probable diagnosis is rheumatoid arthritis. The points in favour of diagnosis are:

1. Small joints involvement (polyarthritis)
2. Bilateral symmetrical distribution
3. Swan-neck deformities with ulnar deviation of hands (deformities).

**895. What is rheumatoid arthritis (RA)?**

**Ans.** Rheumatoid arthritis is an immuno-inflammatory system disorder involving the synovial joints and extra-articular tissue leading to bilateral symmetrical polyarthritis with morning stiffness and extra-articular manifestations.

**896. What are its diagnosis criteria?**

**Ans.** The American College of Rheumatology (ACR) has laid down criteria for diagnosis and classification (Read Clinical Methods in Medicine Vol. I by Prof SN Chugh).

**897. What are the early symptoms and signs in RA?**

**Ans.** The symptoms and signs for early diagnosis of RA are;

1. Insidious onset of polyarthritis with aches and pains in the joints
2. Prolonged morning stiffness (for 6 weeks or longer)
3. Swelling of multiple involved joints for 6 weeks or longer
4. Slowly progressive signs of inflammation of joints, e.g. pain, tenderness, warmth and erythema for > 6 weeks
5. Symmetric joint involvement.

**898. Which are the joints involved in rheumatoid arthritis?**

**Ans.** The joints commonly involved are:

1. *Small joints of hands*, e.g. proximal interphalangeal (PIP) and metacarpophalangeal (MCP) joints are commonly involved. Distal interphalangeal joints (DIP) are rarely involved
2. Wrist joint(s)
3. Elbow joint(s)
4. Knee joint(s)
5. Arthritis of forefoot, ankle and subtalar joints
6. Axial joints (joints of upper cervical spines)

**899. What are extra-articular manifestations in RA?**

**Ans.** They are give in Table 1.188.

**900. What are the causes of anaemia in RA?**

**Ans.** The causes are:

1. Anaemia of chronic disease
2. Iron deficiency (blood loss, NSAIDs)
3. Bone marrow suppression due to drugs used in the treatment (penicillamine, gold, cytotoxic)
4. Folate and vitamin B<sub>12</sub> deficiency
5. Haemolysis caused by drugs.

Anaemia commonly is due to chronic disease and is normocytic normochromic and correlates well with the disease activity.

**901. What are laboratory findings in RA?**

**Ans.** • Normocytic normochromic anaemia

**Table 1.188:** Extra-articular features in RA

<b>I. Systemic</b>
• Fever, weight loss, anorexia, fatigue
<b>II. Musculoskeletal</b>
• Bursitis
• Tenosynovitis
• Muscle wasting
<b>III. Skin</b>
• Rheumatoid nodules
• Vasculitis
• Ulcers and gangrene
• Pyoderma gangrenosa
• Skin – fold infarcts
<b>IV. Eye</b>
• Episcleritis, conjunctivitis
• Sicca syndrome
• Scleritis (scleromalacia)
<b>V. Cardiac</b>
• Endocarditis, myocarditis, pericarditis
• Aortitis, aortic regurgitation (AR)
• Conduction defects
<b>VI. Respiratory</b>
• Pleural effusion
• Bronchiolitis, fibrosing alveolitis
• Nodules
• Caplan's syndrome
<b>VII. Haematological (Reticuloendothelial)</b>
• Anaemia
• Thrombocytosis, eosinophilia
• Felty's syndrome
• Splenomegaly
<b>VIII. Neurological</b>
• Entrapment neuropathy
• Cervical compression
• Peripheral neuropathy
• Mononeuritis multiplex
<b>IX. Miscellaneous</b>
• Amyloidosis
• Systemic vasculitis

- Thrombocytosis, eosinophilia
- Raised ESR
- Raised C-reactive protein
- Raised ferritin concentration as an acute phase protein
- Low serum iron and total iron binding capacity
- Raised serum globulins
- Presence of rheumatoid factor (RF)
- Raised serum alkaline phosphatase activity

**902. What is rheumatoid factor? What is its significance?**

**Ans.** Rheumatoid factors are autoantibodies reactive with Fc portion of IgG.

Significance

- The factor is present in 70% cases of RA
- The factor is not specific as it is present in 5% of healthy persons
- A large number of conditions are associated with presence of rheumatoid factors such as SLE, chronic active hepatitis, sarcoidosis, interstitial pulmonary fibrosis, infectious mononucleosis, hepatitis B, tuberculosis, leprosy, syphilis, SABA visceral leishmaniasis, schistosomiasis and malaria.

**903. What are the causes of polyarthritis?**

**Ans.** The causes are:

1. Rheumatoid arthritis
2. Viral arthritis
3. Juvenile idiopathic arthritis
4. SLE
5. Psoriatic arthritis
6. Generalised/nodular osteoarthritis
7. Metabolic arthritis (hemochromatosis, acromegaly)
8. Gout
9. Pyrophosphate (crystal-induced)
10. Hyperlipidaemia

**Note:** Causes 1 to 6 produce symmetrical involvement while causes 7 to 10 cause asymmetrical polyarthritis.

**904. What are the causes of arthritis involving the small joints and large joints?**

**Ans.** Depending on the joints involvement, the causes are given in Table 1.189.

**905. What is Reiter's syndrome? What are its causes?**

**Ans.** It is an inflammatory reactive arthritis associated with rash, urethritis, conjunctivitis, uveitis and oral ulcers.

Two types are recognised:

1. Following gastrointestinal infection with *Shigella*, *Salmonella*, *Yersinia* or *Campylobacter* (enteric)
2. Following nongonococcal (non-specific) urethritis

**Table 1.189:** Arthritis of small joints and large joints**Small joint arthritis**

- Rheumatoid arthritis
- Reactive arthritis
- Gout
- Enteropathic arthritis
- Nodular osteoarthritis
- Psoriatic arthritis
- SLE
- Metabolic (haemochromatosis)

**Large joint arthritis**

- Reactive arthritis
- Psoriatic arthritis
- Ankylosing spondylitis
- Inflammatory bowel disease associated arthritis

*Note:* Reactive arthritis, enteropathic arthritis and psoriatic arthritis involve both small as well as large joints.

**906. Name the arthritis associated with HLA-B<sub>27</sub>.**

**Ans.** These are as follows:

1. Ankylosing spondylitis
2. Rheumatoid arthritis
3. Reactive arthritis or Reiter's syndrome
4. Post-dysenteric or enteropathic arthritis
5. Psoriatic arthritis.

**907. What is Felty's syndrome?**

**Ans.** It is characterised by chronic RA, splenomegaly, neutropenia and occasionally anaemia and thrombocytopenia (pancytopenia).

**908. What is Caplan's syndrome?**

**Ans.** It is characterised by seropositive rheumatoid arthritis with pneumoconiosis of the lung (nodular opacities with fibrosis). It is commonly seen in coal-miner's.

**909. How will you treat a case of rheumatoid arthritis?**

**Ans.** The aims of treatment are;

- Relief of pain and reduction of inflammation
- Maintenance of function
- Protection of articular structures from damage
- Control of systemic involvement.

**Treatment modalities****1. Medical therapy**

- i. NSAIDs (Cox- I and Cox-2 inhibitors)
- ii. Corticosteroids

- iii. *Disease modifying antirheumatic drugs (DMARDs)*- DMARDs are used early in the disease to modify the course of RA, and to retard the development of erosions or facilitate their healing. The agents used include; gold (IM), antimalarial (chloroquine, hydroxychloroquine), penicillamine, sulphasalazine, antimitotics (methotrexate, azathioprine cyclosporine) and leflunamide
- iv. *Biological agents.* Recently tumour necrosis factors (TNF alpha), blocking monoclonal antibody have been introduced

**II. Surgical treatment**

- Decompression for carpal tunnel syndrome and ulnar nerve involvement
- Synovectomy for persistent synovitis
- Excision arthroplasty
- Arthrodesis
- Joint replacement
- Fixation of joint (for atlanto-axial subluxation)

**910. What are the causes of seronegative arthritis?**

**Ans.** Absence of rheumatoid factor indicates seronegative arthritis. The causes are:

- Ankylosing spondylitis
- Reiter's syndrome (reactive arthritis)
- Arthritis associated with inflammatory bowel disease
- Psoriatic arthritis
- Undifferentiated spondyloarthropathies
- Juvenile chronic arthritis
- Gout and pseudogout.

**911. What is gout and pseudogout? What is gouty arthritis?**

**Ans.** Gout is an inflammatory response to the deposition of monosodium urate monohydrate (MSUM) crystals in the articular and periarticular tissue secondary to hyperuricaemia.

*Pseudogout:* The word pseudogout refers to gout like presentation in calcium pyrophosphate dihydrate (CPPD) crystals induced disease. The crystals evoke an inflammatory response similar to gout. The crystal deposition disease is not a primary disorder but is



secondary to osteoarthritis and is a common occurrence.

**Gouty arthritis:** It may be acute gouty arthritis or chronic erosive, deforming arthritis (tophaceous gout)

**Acute gouty arthritis** is characterised by acute attack of pain involving the big toe (first metacarpophalangeal joint) with fever and chills occurring at night disturbing the sleep of the patient. Arthritis may uncommonly involve other joints also.

**Chronic erosive gouty arthritis** occurs after many years of repeated attacks of acute gout, is characterised by deposition of urate crystals (tophi) in and around the joint leading to joint inflammation, erosion and deformity. The common joints involved are big toe, feet and hand joints.

**912. How will you treat gout?**

**Ans.** The treatment is as follows:

**I. Treatment of acute attack**

- NSAIDs
- Colchicine
- Local and systemic steroids.

**II. Recurrent or chronic gout**

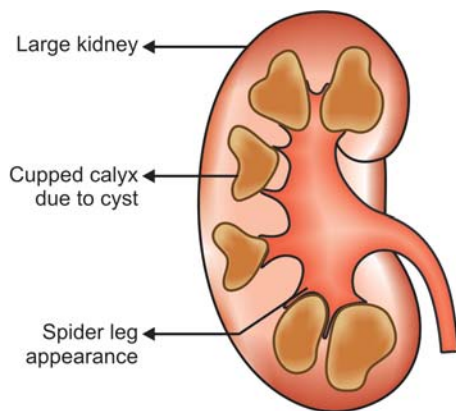
- Reverse the underlying cause of hyperuricaemia, e.g. stop diuretics and alcohol
- Treat associated condition if present, i.e. obesity, hyperlipidaemia, hypertension
- Correct life-style patterns, e.g. avoid high purine diet, exertion, starvation and dehydration
- Lower plasma urate levels either by allopurinol, probenecid or colchicine
- Continue prophylactic doses of colchicine or NSAIDs for few months even after normalisation of hyperuricaemia.

### CASE 67: ADULT POLYCYSTIC KIDNEY DISEASE

A 40-year male patient presented with abdominal pain localised to the flanks with headache and dysuria. There was history of mass in the right side of abdomen. There was no history of fever. There was history of such a disease in the family. Examination revealed hypertension and bilateral palpable kidneys with soft and cystic feel. The USG showed (Fig. 1.67) the enlarged kidneys with multiple cysts in both the kidneys.



**A.** Ultrasonography showing multiple (renal cysts in a patient with adult polycystic kidney disease)



**B.** Diagrammatic representation of features of adult polycystic kidney disease

**Figs 1.67A and B:** Adult polycystic kidney disease (ADPKD)

#### 913. What is probable diagnosis and why?

**Ans.** The probable diagnosis is adult polycystic kidney disease. The points in favour of the diagnosis are;

1. History of flank pain with dysuria
2. Positive family history

3. Presence of hypertension
4. Bilateral palpable kidneys

#### 914. What is adult polycystic kidneys disease (ADPKD)?

**Ans.** Adult polycystic kidney disease is a heredofamilial (autosomal dominant and autosomal recessive) disorder in which cysts are present in kidneys making it palpable and enlarged. These cysts cause compression of the intervening renal tissue and progressive loss of excretory function.

#### 915. What is genetic defect in ADPKD?

**Ans.** Three forms of autosomal dominant genes have been recognised;

1. ADPKD<sub>1</sub> gene accounts for 90% of cases and the gene has been localised to short arm of chromosome 16.
2. ADPKD<sub>2</sub> gene is less common (10%) and is localised to short arm of chromosome 4. These patients develop symptoms and renal failure later than ADPKD<sub>1</sub>.
3. ADPKD<sub>3</sub> gene has been documented but has not been mapped to any specific chromosome

Both ADPKD<sub>1</sub> and ADPKD<sub>2</sub> encode for the polycystins 1 and 2, the mutation of which leads to the disease.

#### 916. What are the cause of pain abdomen in ADPKD?

**Ans.** The causes of acute pain are;

1. Urinary tract obstruction by clot or stone
2. UTI
3. Sudden haemorrhage into a cyst.

#### 917. What is the cause of hypertension in ADPKD?

**Ans.** Hypertension is secondary to intrarenal ischemia from distortion of renal vasculature leading to stimulation of renin-angiotensin – aldosterone system.

#### 918. What are extra-renal manifestations of ADPKD?

**Ans.** These are as follows:

1. Cysts in the other organs, i.e. liver, spleen, pancreas and ovaries. Hepatic cysts are commonest (50-75% cases)

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2. Intracranial aneurysms can occur in 5-10% cases and may bleed leading to subarachnoid haemorrhage
3. Diverticulosis of the colon may occur and patients are more vulnerable to perforation than general population
4. Mitral valve prolapse (25% cases).

### 919. What are the causes of palpable kidney or kidneys?

**Ans.** Read the Clinical Methods in Medicine Vol. I.

### 920. What are the characteristic of renal mass?

**Ans.** The characteristic of renal mass are:

#### *Inspection of abdomen*

- Fullness of renal angle on the side involved

#### *Palpation*

- An irregular mass in lumbar region(s).
- Moves slightly with respiration vertically (up and down)
- Sometimes, bilateral masses are palpable (polycystic kidney disease)
- Soft, cystic or firm in consistency
- Bimanual palpable mass
- Ballotable mass

#### *Percussion*

- A band of resonance elicitable over the mass.

### 921. What are the causes of mass in lumbar region?

**Ans.** Read the "Clinical Methods in Medicine" Vol. I.

### 922. How will you diagnose a case of ADPKD?

**Ans.** Ultrasound is the preferred technique for diagnosis of symptomatic patients and for screening of asymptomatic family members. It has replaced intravenous pyelography (IVP), used to be done previously for diagnosis.

At least 3-5 cysts in each kidney is standard diagnostic criteria for ADPKD

- *IVP*: It has been superseded by *USG*. It detects cysts and distortion of pelvicalceal system and gives typical "Spidery-leg appearance"

- *CT scan*: It is more sensitive than *USG* in detection of small cysts.
- *Genetic linkage analysis*: Genetic probes are available for analysis. The genetic analysis is reserved for cases where radiographic imaging is negative and there is need to confirm the diagnosis, for example, screening of family members for potential kidney donation.

### 923. What are complications of ADPKD?

**Ans.**

- Recurrent urinary tract infection including infection of the cyst (pyocyst)
- Urinary tract obstruction
- Nephrolithiasis (calcium oxalate and uric acid stones) is common
- End-stage renal disease (ESRD) due to progressive decline of renal function is a late complication
- Renal failure.

### 924. How will you treat ADPKD?

**Ans.** As it is genetically related disorder, hence, there is no definite treatment. The aim of treatment is to retard the progress of the disease and preserve renal function as long as possible by:

- Control of hypertension by antihypertensives especially ACE inhibitors
- Treatment of urinary tract infection by appropriate antibiotics
- Relief of chronic pain by an analgesic. If no relief, cyst may be punctured and sclerosed with ethanol.

### 925. What are the causes of renal cysts?

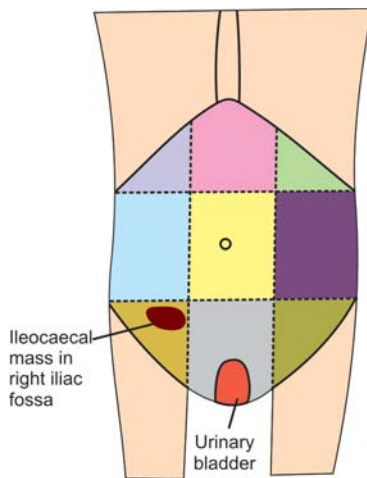
**Ans.** The causes are;

1. ADPKD (autosomal dominant)
2. ADPKD (autosomal recessive)
3. Tuberous sclerosis (Adenoma sebaceum, shagreen patch, benign tumours of CNS, renal angiomyolipomas and renal cysts may occur)
4. *Von Hippel-Lindau disease* (e.g. haemangioblastoma of retina and CNS; bilateral renal cysts may occur)
5. Medullary spongy kidney
6. Medullary cystic disease.

**CASE 68: ILEOCAECAL MASS**

A patient presented with abdominal pain, dull aching in character associated with slight distension of abdomen and constipation. There was normal passage of flatus. Prior to this, patient gave history of off and on alternate diarrhoea and constipation.

Examination revealed dilated loops of gut visible in the central part of abdomen. There was a ill-defined irregular mass palpable in the right iliac fossa (Fig. 1.68A), firm, tender. The abdomen was resonant including the mass on percussion. There were increased bowel sounds on auscultation. The per rectal examination was normal. The barium meals examination of the patient is depicted (Fig. 1.68B).



**Fig. 1.68A:** The site of the mass in right iliac fossa



**Fig. 1.68B:** Ileocaecal tuberculosis. There is narrowing of terminal ileum and caecum is pulled up on barium meal follow through study

**926. What is your probable diagnosis and why?**

**Ans.** The probable diagnosis is subacute intestinal obstruction due to ileocaecal mass. The points in favour are;

- History (dull abdominal pain, central distension and constipation)
- Visible and palpable dilated loops of gut
- Resonant percussion note
- Increased bowel sound

*The mass is ileocaecal because:*

- The mass is in the right iliac fossa
- It is firm, tender and resonant on percussion
- Associated features of subacute intestinal obstruction present.

**927. What are causes of a mass in the right iliac fossa? What are causes of ileocaecal mass?**

**Ans.** Causes of mass in right iliac fossa are:

- An appendicular lump
- An ileocaecal mass (read its causes)
- Ileopsoas abscess
- Gallbladder mass
- Undescended kidney or testis
- Uterine or tubo-ovarian mass.

**Causes of Ileocaecal Mass**

- Hyperplastic ileocaecal tuberculosis
- Amoebic typhilitis
- Carcinoma of caecum and colon
- Inflammatory bowel disease
- Fungal granuloma (aspergilloma)
- Lymphoma
- Impaction of round worms
- Carcinoid tumour.

**928. What are characteristics of ileocaecal tuberculosis?**

**Ans.** These are as follows:

- An irregular firm tender mass that slips under your fingers on palpation
- Symptoms and signs of intermittent subacute intestinal obstruction, e.g. vomiting, distension, constipation, visible gut loops, increased peristaltic sounds

## 272 Bedside Medicine

- History of alternate diarrhoea and constipation, night sweats and low grade fever
- Weight loss, emaciation
- Supportive evidence of tuberculosis elsewhere, e.g. lung, abdominal or cervical lymph nodes, ascites.

*Barium meal study may show pulled up caecum, ulceration and stricture of ileum, multiple areas of dilatation, narrowing and matting of small bowel loops and a filling defect. The study is not to be performed in the presence of subacute intestinal obstruction where barium enema may be done to visualise the filling defect.*

### 929. What are the characteristics of carcinoma of colon?

**Ans.** Read the Clinical Methods in Surgery.

### 930. What are characteristic of amoebic typhilitis?

**Ans.** These are as follows:

- An irregular, firm, tender lump
- Past or present history of amoebic dysentery
- History of pain abdomen and tender descending colon
- Stools are positive for *E. histolytica*.

### 931. What are the characteristics of Crohn's colitis or disease?

**Ans.** These are as follows:

- An inflammatory boggy swelling or mass of adherent loops of intestine. It is soft and tender.
- Associated symptoms such as fever, right quadrant abdominal pain, diarrhoea (often without blood), fatigue and weight loss
- Mild anaemia, aphthous ulceration of mouth, stomatitis, glossitis, cheilosis due to malabsorption may sometimes be seen.
- There may be associated anorectal complications such as fistulae, fissures and perirectal abscess
- Extracolonic manifestations such as arthritis may also occur
- Sigmoidoscopy and radiological studies are important for diagnosis. Barium meal study may show *cobble-stone appearance* of the mucosa and fistulous tracts. Barium enema may reveal rectal sparing, presence of skip lesions, small

ulcerations occurring on small irregular nodules. Fibreoptic colonoscopy and mucosal biopsy will confirm the diagnosis.

### 932. What are the characteristics of an appendicular lump?

**Ans.** These are as follows:

- An irregular, firm, tender lump often fixed but may show slight mobility.
- History of recurrent attacks of periumbilical pain with vomiting, settling down to the right lower quadrant
- Fever and leucocytosis
- Guarding and muscular rigidity on palpation
- Rebound tenderness may be present, indicates peritoneal inflammation around the appendix
- Positive Rovsing's and psoas sign
- Obturator sign may be positive
- USG of abdomen may help in the diagnosis.

### 933. What are clinical presentation of abdominal tuberculosis?

**Ans.** These are:

1. Ascites due to tubercular peritonitis
2. Ileocecal tuberculosis, e.g. hyperplastic and ulcerative
3. Tuberculosis of lymph node (tabes mesenterica)
4. Tuberculous abscess, e.g. liver and spleen.

### 934. What are the clinical presentation of intestinal tuberculosis?

**Ans.** These are as follows:

- I. Nonspecific symptoms of pain abdomen, low grade fever with evening rise, night sweats, decreased appetite and weight loss. The abdominal examination may show dilated loops of gut with doughy feel.
- II. Patients may present with symptoms and signs of subacute intestinal obstruction. These are due to multiple areas of narrowing.
- III. Diarrhoea and malabsorption. Diarrhoea is common in ulcerative type of tuberculosis. Blood and frank pus in the stool is rare. The malabsorption in intestinal tuberculosis is due to decreased absorptive surface area as a result of;
  - Extensive ulceration



- Lymphatic obstruction
  - Bacterial overgrowth (Blind loop syndrome)
- IV. Acute intestinal obstruction due to stricture formation
- V. Perforation and fistula formation is rare in intestinal tuberculosis.

**935. What is carcinoid tumour and carcinoid syndrome?**

**Ans.** Carcinoid tumour originates from enterochromaffin cells (APUD cells) of the intestine and the sites being appendix, terminal ileum and rectum. Clinically it is asymptomatic until they metastasise in the liver and produce carcinoid syndrome.

The carcinoid syndrome is characterised by;

- Bluish-red flushing on face and trunk due to vasodilatation occurring spontaneously or during an attack of pain abdomen
- Gastrointestinal hurry producing pain and recurrent watery diarrhoea
- Cardiac abnormalities, e.g. pulmonary stenosis and tricuspid incompetence
- Bronchial carcinoid produces recurrent attacks of wheezing
- Hepatomegaly due to metastases in symptomatic patients.

# 2

## Bedside Procedures and instruments

### LUMBAR PUNCTURE (LP)

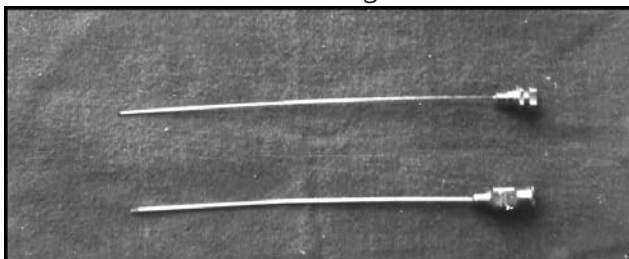
It is a bedside procedure done to remove cerebrospinal fluid (CSF) from the subarachnoid space by puncturing it at or below L<sub>2</sub>-L<sub>3</sub> intervertebral space. The spinal cord ends at the level of L<sub>1</sub> vertebra after which there is a *cul-de-sac* (dilatation of subarachnoid space) from which CSF can be removed. The instrument used for the purpose is called *lumbar puncture (LP) needle* (Fig. 2.1).

#### Indications

##### I. Diagnostic

CSF is removed for diagnosis of the following conditions:

- i. *CNS infections/inflammation*
  - Encephalitis
  - Meningitis
  - Multiple sclerosis
  - Myelitis
  - Acute post-infective polyneuritis (Guillain-Barre syndrome)
- ii. *Subarachnoid haemorrhage (to be done after fundus examination)*
- iii. *Infiltrative conditions*
  - Carcinomatous meningitis



**Fig. 2.1:** Lumbar puncture needle; Stilet (upper) and needle (lower)

- Lymphoma and leucaemic infiltration of meninges
- iv. *To confirm raised intracranial pressure when CT scan excludes the danger of brain-stem herniation*
  - Benign raised intracranial tension
  - Cerebral venous sinus thrombosis
- v. *Instillation of contrast media or an isotope*
  - Myelography (CT myelography)
  - Cisternography.

##### II. Therapeutic

Lumbar puncture is done for treatment purpose;

- i. Administration of intrathecal antibiotics or tetanus immunoglobulin
- ii. Administration of antileucaemic drugs in ALL
- iii. Spinal anaesthesia
- iv. Removal of CSF to lower the pressure in benign intracranial hypertension

##### III. Other uses of LP needle

- i. Used as aspiration needle for tapping fluids from a cavity, e.g. ascites, pleural effusion.

#### Contraindications

- i. Thrombocytopenia and coagulation disorders
- ii. Depressed consciousness especially if focal neurological signs present. CT scan to be done initially to rule out raised intracranial pressure or mass lesion. LP should not be performed in presence of raised intracranial pressure or a mass lesion
- iii. Papilloedema

- iv. Skin infection at the site of lumbar puncture. It is not a contraindication, LP can be done one space higher
- v. Lumbar meningocele.

Normal CSF and findings in meningitis are given in Table 2.1.

### Complications

- *Brainstem herniation or cerebellar coning*: To avoid this LP should not be done in presence of gross papilloedema. In dire emergency, slow removal of CSF by keeping the stillet inside the needle is advised and signs of brainstem herniation to be looked for (change in size of pupil).
- *Introduction of infection*: To avoid it, aseptic precautions are to be followed.
- *Postspinal headache*: Measures to avoid/treat it are;
  - i. Remove the fluid slowly
  - ii. Put the needle obliquely into subarachnoid space

- iii. Put the patient in prone position if headache develops.

### Procedure

#### Site— $L_3$ - $L_4$ Interspace

1. The patient is placed on the edge of the bed or a table in the left lateral position with knees drawn upto the abdomen and neck is gently flexed so as to bring them as close as possible.
2. The 3rd and 4th lumbar spines are palpated by rolling the fingers on the spine. The 4th lumbar spine usually lies on a line joining the iliac crests and  $L_3$  is just above it. The interspace between  $L_3$  and  $L_4$  is defined.
3. Under aseptic precaution, local infiltrative anaesthesia (xylocaine 2%) is used at the site of puncture ( $L_3$ - $L_4$ ).
4. The LP needle is pushed through the skin in the midline, it is pressed steadily forwards and slightly towards the head. When the needle is felt to penetrate the duramater (a sudden release of resistance), the

**Table 2.1:** Differential diagnosis of CSF findings in meningitis

Finding	Pyogenic meningitis	Tubercular meningitis	Viral meningitis	Fungal meningitis	Carcinomatous meningitis
Gross appearance	Turbid	Clear or straw coloured, cob-web seen on standing	Clear	Clear	Clear or haemorrhagic
CSF pressure	Elevated	Elevated	Normal	Elevated	Elevated
Proteins	Elevated (>45 mg/dl)	Elevated	Normal or slightly elevated	Elevated	Elevated
Glucose	Markedly reduced (<30 mg/dl)	Moderately reduced (< 40 mg/dl)	Normal	Reduced	Normal
Cells	>1000 cells/ml mainly polymorphs	>400 cells/ml mainly mono-nuclear	25-500 cells/ml mainly lymphocytes	Mononuclear or lymphocyte pleocytosis	Malignant cells may be seen
Isolation of organism	Gram's stain is positive	Acid fast stained smear positive in 10-40% cases	Not possible	India-ink or fungal wet mounts of CSF positive	—
PCR for detection of DNA sequence	Detection of bacterial DNA is just research test	<i>M. tuberculosis</i> DNA positive in 70-80% cases	Viral specific DNA or RNA from CSF positive	Cryptococcal antigen is specific and positive	—
Culture	Positive in >80% cases	Positive <50% cases. It is a gold standard to make diagnosis	Viral culture results disappointing because of cumbersome procedure	Positive for fungi	—

stilet is withdrawn and a few drops of CSF are allowed to escape.

5. The CSF pressure can be measured by connecting a manometer to the needle. The normal CSF pressure is 60-150 mm H<sub>2</sub>O. It rises and falls with respiration and heart beat.
7. Specimens are procured in three sterile vials/tubes and sent to laboratory. An additional sample in which sugar level can be measured together with simultaneous blood sugar sample should be taken when relevant (e.g. meningitis).
8. Now the needle is removed, the site is sealed with a wisp of cotton soaked in tincture. The patient is made to lie flat to avoid a postspinal headache.

#### *Dry Tap*

It means CSF does not come out through the LP needle, could be due to:

1. Improper positioning of the needle, i.e. needle is not in the subarachnoid space. This is common cause.
2. Subarachnoid space is obliterated by a tumour or adhesive arachnoiditis.

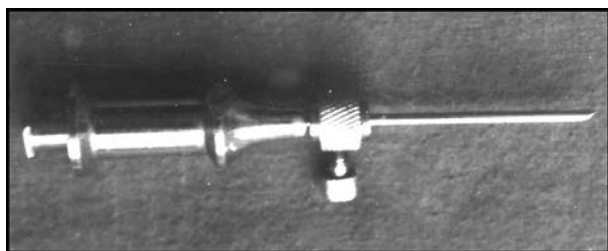
### **BONE MARROW ASPIRATION**

It is done in adults to aspirate the marrow from sternum or posterior iliac crests because of being superficial and accessible (all flat bones and vertebrae contain bone marrow in adults). If aspiration fails then a trephine bone marrow biopsy is done, if necessary. The instrument used in the procedure is bone marrow aspiration needle (Fig. 2.2).

#### **Indications of Bone Marrow Aspiration**

##### **1. Bone marrow infiltration**

- Leucaemia/lymphoma



**Fig. 2.2:** Bone marrow aspiration needle

- Secondary carcinoma
- Myelofibrosis/agnogenic myeloid metaplasia

##### **2. Cytopenias**

- Neutropenia
- Thrombocytopenia
- Anaemias including aplastic
- Pancytopenia

##### **3. Myeloproliferative disorders**

4. **Infections**, e.g. bone marrow aspirate is used for culture of typhoid, tuberculosis, where other tests are negative but suspicion is high.

#### **Contraindications**

- Severe thrombocytopenia (count <20,000/ $\mu$ l) or a coagulation defect
- Osteomyelitis/infection at the site of puncture.

#### **Complications**

- Bone pain
- Haemorrhage
- Infection.

#### **Procedures**

Site—Mid-manubrium sterni region in adults and iliac crest in children.

1. The patient is made to lie flat on the bed and skin is shaved over the sternum.
2. The site is cleansed with antiseptic solution many times.
3. The site is infiltrated with local anaesthesia under aseptic precaution.
4. The bone marrow needle is introduced at the site vertically and bone marrow is aspirated with the help of syringe attached to the needle.
5. Make the smear of bone marrow on the slide by discarding or shedding off the peripheral blood and send it for examination.
6. Remove the needle, paint the site with a cotton wisp soaked with tincture benzoin.

#### *Dry Tap*

No bone marrow aspirated when the needle is in place. It could be due to:

1. Faulty technique.
2. Myelofibrosis, e.g. marrow replaced by fibrosis
3. Marrow packed tightly with infiltrates, hence, is difficult to aspirate.

### TISSUE BIOPSY NEEDLE

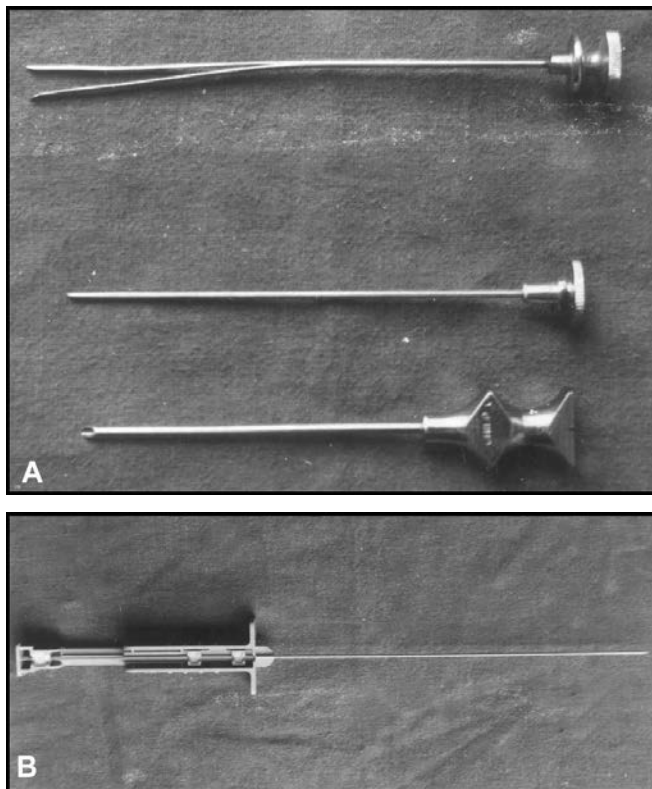
Biopsy means taking a small amount of tissue percutaneously from the intact organ with the help of a needle called tissue biopsy needle (Figs 2.3A and B). The *Vim-Silverman's needle* (A) is more traumatising than *trucut needle* (B), which is a disposable needle.

#### Uses

It is used to take the biopsy from kidney, liver, pleura in diseased state for diagnosis and differential diagnosis.

#### Liver Biopsy

Liver biopsy is now performed under ultrasound or CT guidance particularly when specific lesions need to be biopsied.



**Figs 2.3A and B:** Tissue biopsy needles:  
A. Vim-Silverman B. Trucut (disposable)

Laparoscopic guided liver biopsy is done through a small incision in the abdominal wall under local anaesthesia.

A transjugular approach is used when liver biopsy is essential but coagulation studies prevent percutaneous approach.

#### Indications

1. Unexplained hepatomegaly or hepatosplenomegaly
2. Chronic hepatitis and cirrhosis of the liver
3. Persistently abnormal liver function tests
4. Suspected systemic or infiltrative disease, e.g. sarcoidosis, miliary tuberculosis or fever of unknown origin (PUO), Wilson's disease
5. Suspected primary or metastatic liver tumour
6. Screening the relatives of patients with certain diseases, e.g. haemochromatosis
7. Operative biopsy may sometimes be valuable as in the staging of lymphoma.

#### Contraindications

- Uncooperative patient or patient who refuses to give a written consent.
- Impaired haemostasis (prothrombin time prolonged by 3 sec or more over control or PTT or BT prolonged and platelet count less than  $80 \times 10^9/L$ ).
- Tense ascites.
- Extrahepatic cholestasis.
- When there is possibility of a hydatid cyst.

#### Complications

- Haemorrhage
- Infection
- Pleurisy, perihepatitis producing shoulder and abdominal pain
- Biliary peritonitis.

#### Renal Biopsy

##### Indications

- Asymptomatic proteinuria ( $>1$  g/day) or haematuria (occasional indication).
- Adult nephrotic syndrome. In nephrotic syndrome in children, it can be done only if proteinuria persists after a trial of steroids.



- Unexplained renal failure where kidneys are normal-sized on ultrasound.
- Failure to recover from assumed reversible acute renal failure.
- Systemic disease with renal involvement, e.g. SLE, sarcoidosis, amyloidosis (occasional).

#### Contraindications

- Uncooperative patient or patient who refuses to give a written consent.
- Single kidney
- Small contracted kidneys (technically difficult, histology is difficult to interpret and prognosis remains unaltered).
- Bleeding diathesis.
- Uncontrolled hypertension.
- Perinephric abscess or pyonephrosis, hydronephrosis or polycystic kidney disease.

#### Complications

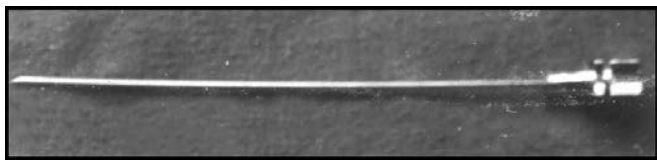
- Macroscopic haematuria (about 20%).
- Pain in the flank, sometimes referred to shoulder tip.
- Perirenal haematoma.
- Transient AV fistula or aneurysm formation.
- Introduction of infection.

### Pleural Biopsy

It is done always in the presence of pleural effusion for diagnosis and differential diagnosis.

### ASPIRATION (PARACENTESIS)

Paracentesis means aspiration of fluid accumulated in one of the serous cavities. It is done to remove the excess of fluid with the help of a wide bore needle called *aspiration needle* (Fig. 2.4). Excess of fluid can accumulate under pathological conditions in pleural



**Fig. 2.4:** Aspiration needle

cavity (pleural effusion/empyema) or pericardial cavity (pericardial effusion) and peritoneal cavity (ascites).

### Paracentesis of Pleural Fluid

#### Indications

##### A. Diagnostic

- For diagnosis and differential diagnosis of pleural effusion, e.g. transudate or exudate.
- Tubercular pleural effusion when fever and toxemia not subsiding after 4 weeks of anti-tubercular therapy.

##### B. Therapeutic

- To relieve dyspnoea, if there is cardiorespiratory embarrassment.
- Empyema thoracis: If fluid removed on first occasion is pus, then intercostal drainage with the help of self-retaining tube/catheter should be attempted.

#### Complications

- Pulmonary oedema may develop with sudden removal of a large amount of fluid. It is rare.
- *Hydropneumothorax (iatrogenic)*: Air may be sucked into pleural cavity during the procedure, hence X-ray chest to be done after aspiration.

### Paracentesis of Ascites (Ascitic Tap)

#### Indications

- For diagnosis and differential diagnosis of ascites. About 20-50 ml of fluid is removed.
- Tense ascites producing cardiorespiratory embarrassment; fluid (2-3 L) is removed to relieve dyspnoea.

#### Complications

- Leakage of ascitic fluid (continuous soaking of clothes)
- Introduction of infection
- Repeated frequent tapping may result in anaemia, hypoproteinaemia.

### Paracentesis of Pericardial Fluid

#### Indications

- For diagnostic purpose to determine the nature of fluid. About 20-50 ml of fluid is removed.
- Cardiac tamponade to relieve dyspnoea. Fluid is removed as much as possible.

#### Complications

- Haemorrhage or bleeding
- Infection
- Injury to liver or diaphragm if subcostal approach is used to remove the fluid.
- Shoulder pain.

### Tapping of Liver Abscess

Liver abscess is mostly amoebic but could be pyogenic in origin. Tubercular abscess is rare.

#### Indications

Liver abscess is tapped under following situations:

1. When pyogenic origin of the abscess is suspected. It is tapped to differentiate amoebic from pyogenic abscess.
2. A large left lobe abscess (> 10 cm).
3. *Impending rupture*: Abscess should be tapped irrespective of its size, if it is superficial and poses a danger to rupture.
4. Abscess not responding to treatment.

### TRACHEOSTOMY

Tracheostomy means opening of the trachea to the surface through which a tracheostomy tube (Fig. 2.5) is



Fig. 2.5: Tracheostomy tube

inserted and cuffed to maintain ventilation and to aspirate the secretions.

#### Indications

1. In unconscious patients with depressed pharyngeal or cough reflexes, e.g. neuromuscular respiratory paralysis.
2. In tetanus to maintain ventilation.
3. In laryngeal/pharyngeal obstruction (nasopharyngeal carcinoma, diphtheria).
4. Systemic anaphylaxis and angioedema when patient becomes cyanosed.

#### Complications

##### Early

- Surgical complications, e.g. haemorrhage, pneumothorax.
- Subcutaneous emphysema.

##### Intermediate

- Erosion of tracheal cartilage.
- Erosion of innominate artery.
- Infection.

##### Late

- Tracheal stenosis
- Collapse of tracheal rings at the level of stoma.

### ENDOTRACHEAL INTUBATION

It refers to putting the endotracheal tube (Fig. 2.6) into the trachea through laryngeal opening via mouth.

#### Indications

It is done for respiratory support.

1. Cardiorespiratory arrest.
2. Acute respiratory failure.
3. Prophylactic postoperative ventilation in poor risk patients with depressed respiration and profuse secretions.
4. During general anaesthesia.
5. Head injuries producing unconsciousness and depressed respiration.



**Fig. 2.6:** An endotracheal tube

6. Chest injuries/lung contusion.
7. Respiratory depression in poisoning.
8. Systemic anaphylaxis and angioedema when patient is cyanosed.

### Complications

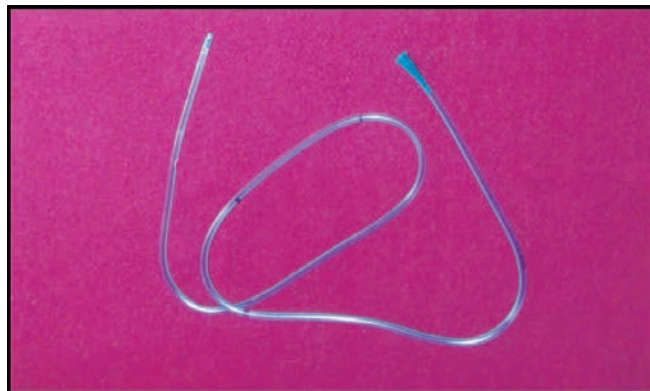
- Tube may slip into one of the bronchus or in oesophagus.
- Migration of the tube out of trachea.
- Obstruction of the tube due to kinking or secretions.
- Mucosal oedema and ulceration of trachea due to tube.
- Damage to cricoarytenoid cartilage.
- Tracheal stenosis (late complications).

### NASOGASTRIC INTUBATION (RYLE'S TUBE INTUBATION)

Ryle's tube (Fig. 2.7) is a fine bore rubber or plastic-silicon tube used for nasogastric intubation. The tube is passed intranasally or through the mouth into the stomach, the position of which is confirmed either by passing the air through the tube into stomach and simultaneous hearing of hussing sound by stethoscope or by aspiration of food material or by X-ray.

### Indications

1. *Nutritional supplementation:* It is used in hospitalised patients for internal feeding required in those patients who cannot eat, should not eat, will not eat or cannot eat enough, such as:
  - Unconscious patients
  - Neurological dysphagia (dysphagia without oesophageal obstruction)



**Fig. 2.7:** Nasogastric (Ryle's) tube.

(The tube for adult is a long fine bore (30 inches) with distal end blind containing oval bulb and has side-holes. It is passed by this end through nose into stomach. The proximal end is open to which syringe is attached. From proximal to distal end it has four marks indicating end of oesophagus, cardia of stomach, pylorus of stomach, and the duodenum)

- Post-traumatic or postoperative or post-radiation weakness
  - In patients with burns.
2. Nutritional support (Ryle's tube feeding) for mal-nourished children/adults.
  3. For gastrointestinal decompression in acute intestinal obstruction, paralytic ileus (perforation), haemorrhage and acute pancreatitis.
  4. Gastric lavage in patients with drug overdose or poisoning.
  5. To remove fluid for gastric analysis.
  6. For drug delivery in unconscious patients.
  7. For diagnosis of acute oesophageal or gastric bleed.

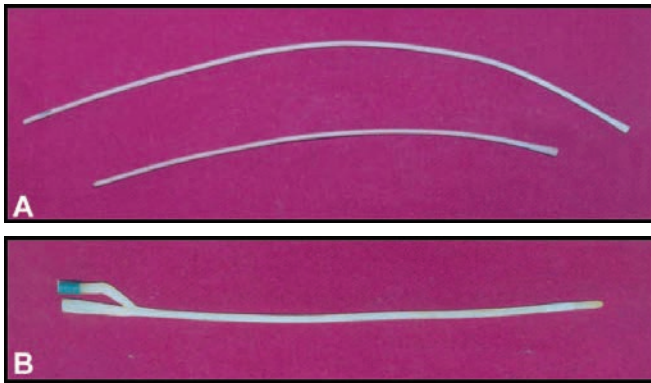
### Complications

#### Immediate

- Regurgitation and aspiration of gastric contents into lung (pneumonia)
- Blockage of the tube.

#### Late (prolonged use)

- GI side-effects, the most common being diarrhoea
- Metabolic complications after prolonged feeding including hyperglycaemia, hyperkalaemia as well as low levels of potassium, magnesium, calcium and phosphate



**Figs 2.8A and B:** Urinary catheters: (A) Simple rubber catheter (Upper – Large; Lower – Small), (B) Self-retaining catheter (Foley's)

- Ulceration of nasal and oesophageal tissues leading to stricture formation.

## URINARY CATHETERISATION

It is a method to remove the urine from the urinary bladder by passing a catheter (Figs 2.8A and B) through the urethra. Catheterisation may be done just once or repeatedly by a simple catheter or continuously by putting a self-retaining catheter for few days.

### Indications or Uses

*Catheterisation just once (by simple catheter)*

- Retention of urine due to reversible cause
- Before or during delivery
- To differentiate anuria from retention of urine
- To obtain urine specimen from an unconscious patient
- To differentiate pelvic swelling from distended bladder
- Before cystoscopy.

*Continuous urinary drainage (by self-retaining catheter)*

- Unconscious patient
- Peripheral circulatory failure to monitor urinary output
- Paraplegia with bladder involvement (incontinence or retention of urine)
- Neurogenic bladder
- Inoperable prostatic carcinoma.

*Other uses*

- For cystography
- Simple catheter can be used as a tourniquet, as a stent or as a sling

### Contraindications

- Acute urethritis

### Complications

- Haemorrhage
- Creation of false passage
- Introduction of infection
- Blockage of urethra leading to retention
- Urethral ulceration and stricture formation on prolonged use.

### Precaution

- Self-retaining catheter should be irrigated with an antiseptic solution daily
- Self-retaining catheter preferably be changed after few days
- Urine culture and sensitivity may be done when patient develops unexplained fever.

## OXYGEN DELIVERY DEVICES

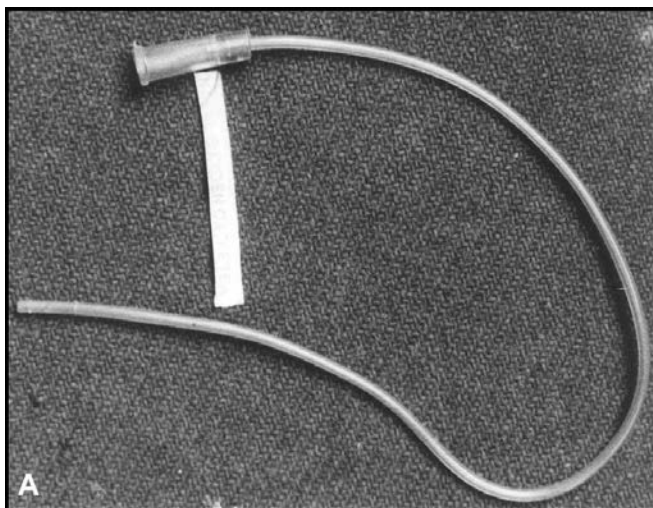
Oxygen can be delivered by many devices such as nasal catheter, simple face-mask and venturi-mask (fixed-performance device) to spontaneously breathing patients. Oxygen is initially given either by nasal catheter or via face-masks (Figs 2.9A to C).

In majority of patients, except COPD with  $\text{CO}_2$  narcosis, the concentration of  $\text{O}_2$  given is not important and  $\text{O}_2$  can be given by simple nasal catheter or face mask (Figs 2.9A and B). With these devices,  $\text{O}_2$  concentration varies from 35-55% with  $\text{O}_2$  flow rates between 6-10 L/min. Nasal catheter or simple face mask are often preferred because they are less troublesome and do not interfere with feeding or speaking. Fixed performance mask (venturi mask – Fig. 2.9C) is used in patients with COPD with elevated  $\text{PaCO}_2$  (type II respiratory failure) where concentration of  $\text{O}_2$  delivered is very important and through this the desired concentration of  $\text{O}_2$  can be delivered and controlled.

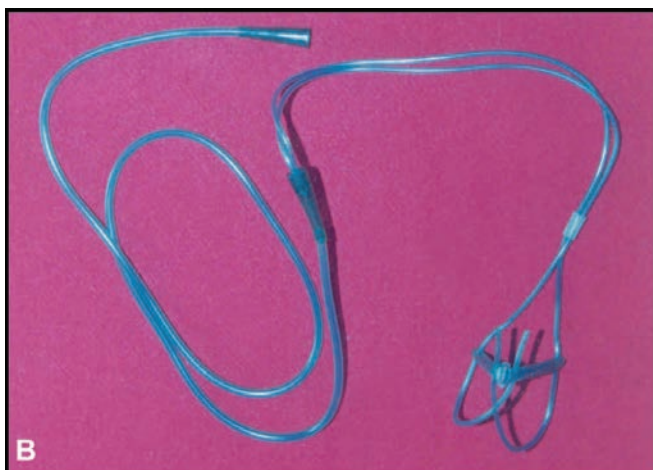
### Indications of Oxygen Therapy

- Type I (hypoxaemic) respiratory failure
- Type II (hypercapnic) respiratory failure (COPD with acute exacerbation)

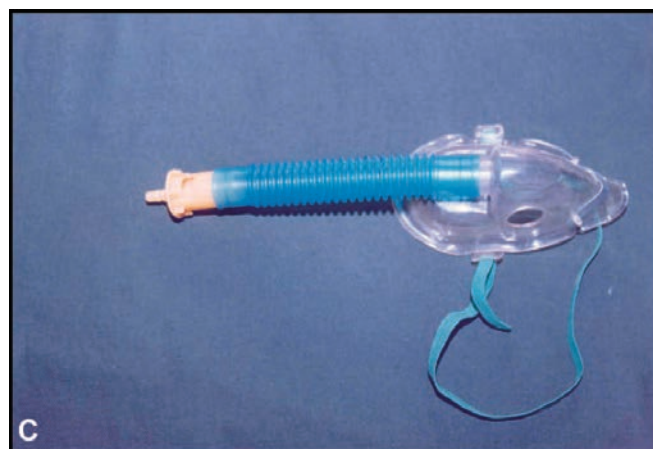




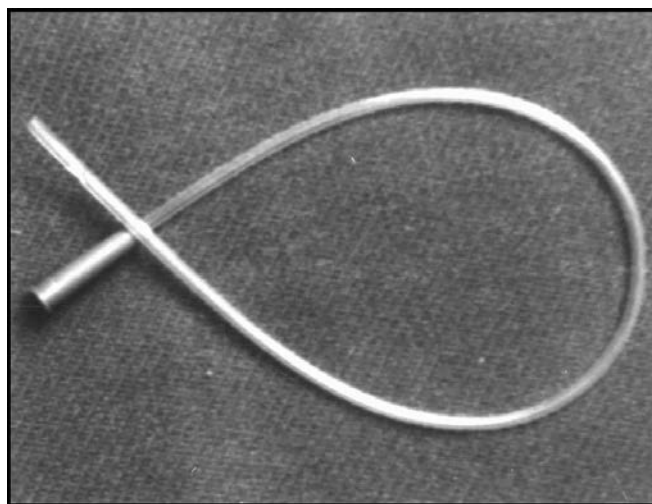
**Fig. 2.9A:** Nasal oxygen catheter (holes at the end)



**Fig. 2.9B:** Nasal oxygen set



**Fig. 2.9C:** Venturi mask (masks are available to deliver 24%, 28% and 35% O<sub>2</sub>)



**Fig. 2.10:** Nasopharyngeal suction catheter

*Note:* Simple urinary catheter, nasopharyngeal suction catheter and simple nasal catheter can be confused with each other. Note the following:

1. Simple urinary catheter is wide bored rubber tube with a hole on the side at distal end
2. Nasal oxygen catheter is a narrow lumen rubber catheter open on both the ends with many side holes at the distal end
3. Suction catheter is a narrow bored plastic catheter with a hole on one side, and on the tip

- Shock
- Asphyxia (e.g. hanging)
- Acute myocardial infarction
- Cardiac tamponade
- Acute severe asthma/status asthmaticus
- Acute pulmonary oedema
- Tension pneumothorax
- Carbon monoxide poisoning.

### Complications

- Damage to the lung leading to acute pulmonary oedema. This is due to liberation of O<sub>2</sub> free radicals due to hyperoxia (high concentration of O<sub>2</sub>).

### NASOPHARYNGEAL SUCTION CATHETER

It is a small lumen rubber or plastic catheter having holes on the sides for entry of secretion. It is blind at distal end, the proximal end is connected to the suction apparatus (Fig. 2.10).



### Indications for Suction

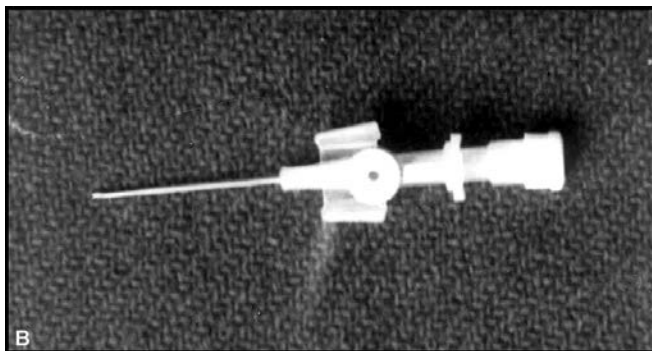
- Unconscious patient
- Tetanus (through tracheostomy tube)
- Cardiac arrest. It is done during cardiopulmonary resuscitation
- Excessive bronchial secretion during drug overdoses or poisoning (organophosphorus compounds)
- Respiratory failure to maintain clear airways
- Drug anaesthesia, surgery and postoperatively.

### INTRAVENOUS LINE ACCESS (IV ACCESS)

To procure IV line and its preservation is an important and preliminary step in management of dehydration, shock, cardiac arrest and any unconscious patient. The IV line can be procured and maintained by simple needle, scalp vein set (Fig. 2.11A) and by cannula (Branula Fig. 2.11B).

#### Indications

1. **Emergency:** It should be procured on urgent basis during following conditions:



**Figs 2.11A and B:** (A) Scalp vein set, (B) Cannula (Branula)

- Cardiac arrest
- Shock
- Unconscious or comatose patient
- Diabetic ketoacidosis or hypoglycaemic coma
- Acute gastroenteritis and pancreatitis
- Acute dehydration or fluid loss/blood loss.

#### 2. Immediate

- Acute attack of bronchial asthma
- Respiratory failure
- Anaphylactic reactions
- Acute myocardial infarction
- Thyrotoxic crisis
- Hypercalcaemic crisis
- Poisoning.

#### 3. Others

- For drug administration
- For fluid therapy who is not accepting orally, or for nutritional support during therapy for cancer, fistulae and severe inflammatory bowel disease
- Forced diuresis
- For transfusion of blood and blood products
- Dialysis.

### Complications

- Thrombophlebitis
- Pain at the site of puncture
- Introduction of infection
- Transmission of hepatitis or AIDS.

### INTRAVENOUS INFUSION SET

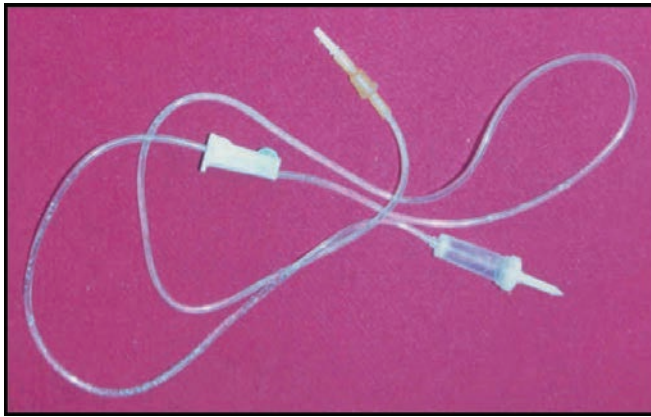
It is transmission line containing a bulb near the proximal end to see the rate of flow. At one end it has a plastic nozzle for connection to the bottle or bag. At the other end, it is connected to intravenous line (Fig. 2.12).

#### Indications

- For transfusion of fluids, crystalloid and colloids
- For blood or blood product transfusion.

### MOUTH GAG

It is a wide noncompressible transparent tube with a wide hole (Fig. 2.13) to maintain patent airway during anaesthesia and in an unconscious patient as tongue may fall



**Fig. 2.12:** Intravenous infusion set

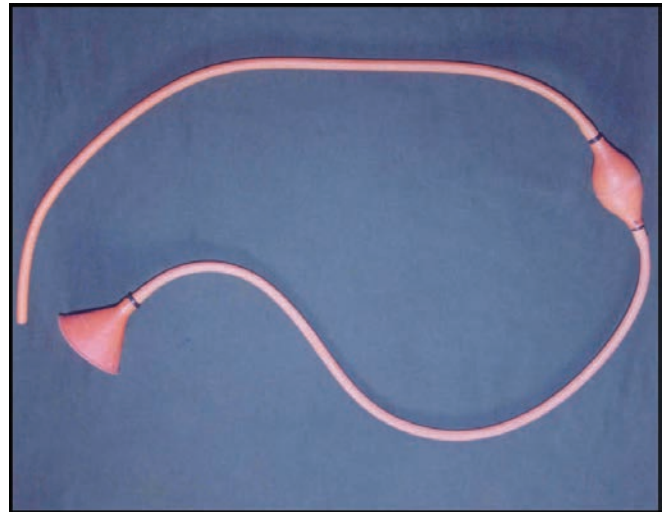


**Fig. 2.13:** Mouth gag

back on oropharynx and may obstruct respiratory airway during anaesthesia or unconsciousness.

#### Indications

1. To prevent falling of tongue during repeated attacks of epilepsy or status epilepticus. It also protects the tongue from injury during these episodes.



**Fig. 2.14:** Gastric (stomach) lavage tube

2. To prevent falling of tongue in an unconscious patient.
3. To maintain patent airway prior to endotracheal intubation.

#### STOMACH (GASTRIC) LAVAGE TUBE

This is a wide bore rubber tube having a cup at one end for entry and exit of fluid. There is a bulb in the middle. The other end (gastric end) lies in the stomach (Fig. 2.14).

#### Indications

- Gastric lavage is attempted in poisoning or drug overdose.

#### Contraindications

- Corrosive poisoning  
*Note:* Ryle's tube can be used for gastric lavage also.

# 3

## Commonly Used Drugs

### DRUGS USED IN CARDIOLOGY

#### CARDIOVASCULAR DRUGS

Categorisation of drugs used in disorders of cardiovascular system is:

#### CARDIAC STIMULANT

- Cardiac stimulants, e.g. glycosides, (digoxin, digitoxin, anabine) and amrinone (inamrinone). They are discussed in Table 3.1.
- Sympathomimetic amines e.g. noradrenaline, adrenaline, isoproterenol (isoprenaline), dopamine and dobutamine. They have been dealt separately.

#### ANTI-ARRHYTHMIC DRUGS

(Vaughan William classification (Table 3.2))

##### **Class I (Block Na Channels)**

**1A:** Drugs that reduce  $V_{max}$  and prolong action potential duration

- Quinidine
- Procainamide
- Disopyramide

**1B:** Drugs that do not reduce  $V_{max}$  but prolong action potential duration

- Mexiletine
- Phenytoin
- Lidocaine
- Tocainide

**1C:** Drugs that reduce  $V_{max}$ , primarily slow conduction and can prolong refractoriness

- Flecainide
- Propafenone
- Moricizine

##### **Class II: Betablockers (block beta-adrenergic receptors)**

- Propranolol, metoprolol, alenolol, timolol, oxyprenolol, sotalol, bisoprolol, nebivolol, carvedilol

##### **Class III: Drugs block potassium channels and block multiple phases of the action potential and prolong repolarisation**

- Amiodarone, sotalol, bretylium and N-acetylprocainamide, ibutilide, dofetilide

##### **Class IV: Calcium channel blockers**

- Diltiazem, verapamil and others

##### **Other antiarrhythmic drugs**

- Adenosine
- Digitalis

#### Betablockers

Beta receptors can be separated into two categories; (i) that affect the heart ( $\beta_1$ ) and (ii) that affect predominantly blood vessels ( $\beta_2$ ) or the bronchi. Therefore  $\beta_1$  receptors produce cardiac stimulation and  $\beta_2$  receptors produce bronchodilation and vasodilation. Cardioselective  $\beta_1$  blockers antagonise the  $\beta_1$ -cardiostimulatory effects and have less effect on  $\beta_2$ -responses. Nonselective-beta blockers antagonise the effects of both  $\beta_1$  and  $\beta_2$  receptors. At high doses, even selective betablockers also block  $\beta_2$  receptors.

Some betablockers (alprenolol, oxyprenolol, pindolol) possess “intrinsic sympathomimetic activity” i.e. they slightly activate the  $\beta$ -receptors. These drugs are as efficacious as other betablockers without intrinsic sympathomimetic activity and may cause less slowing of heart

Table 3.1: Cardiac stimulants

Drug	Mechanism of action	Uses	Dose	Side effects	Special remarks
1. Cardiac stimulants Digoxin	<ul style="list-style-type: none"> <li>Positive inotropic effect in normal, nonfailing hypertrophied and failing hearts</li> <li>Negative chronotropic effect (slows conduction through AV node by increasing effective refractory period by an enhanced vagal effect)</li> <li>It enhances excitability, automaticity and ectopic impulse formation</li> </ul>	<ul style="list-style-type: none"> <li>CHF</li> <li>To slow the ventricular response in atrial fibrillation and atrial flutter</li> <li>To terminate PSVT</li> </ul>	<p>Oral: Loading dose 0.25-0.5 mg stat then 0.25 mg every 4 hr <math>\times</math> 2 doses</p> <p>Maintenance dose (0.25 mg on alternate days or 5 days in a week)</p> <p>IV Loading dose: 0.25-0.5 mg slow IV bolus, then 0.25 mg IV after 2-4 hours, then followed by oral drug.</p>	<p>1. Early: Anorexia, nausea, vomiting due to effect of drug on medullary centres.</p> <ul style="list-style-type: none"> <li>Cardiac e.g. VPCs, bigeminy rhythm, nonparoxysmal SVT with block (Wenckebach), ventricular tachycardia, ventricular fibrillation</li> <li>Sinus arrhythmias, (sinus arrest, SA blocks), AV junctional and multifocal or bidirectional VT</li> </ul> <p>2. Chronic intoxication</p> <ul style="list-style-type: none"> <li>Exacerbation of heart failure, weight loss, cachexia, neuralgias, gynaecomastia, yellow vision, delirium</li> </ul>	<ul style="list-style-type: none"> <li>Avoid administration within 2 hours of antacid</li> <li>May be proarrhythmic</li> <li>Monitor K<sup>+</sup> and correct hypovolemia</li> <li>Its serum level increase with verapamil, quinidine and amiodarone</li> <li>For digitalis induced arrhythmias use phenytoin, or a betablocker or lidocaine</li> <li>Fab antibodies are used for severe intoxication</li> </ul>
Amrinone	<ul style="list-style-type: none"> <li>Positive inotropic effect (increases CO), vasodilator agent (decreases preload and afterload)</li> </ul>	<p>Short-term management of CHF in patients unresponsive to digitalis, diuretics and vasodilators</p>	<p>IV Loading dose: 0.75 mg/kg over 2-3 min, may be repeated after 30 min</p> <p>Maintenance infusion 5-15 <math>\mu</math>g/kg/min (dose titrated according to response). Do not exceed 10 mg/kg in a day</p>	<ul style="list-style-type: none"> <li>GI tract symptoms e.g. nausea, vomiting, pain abdomen, anorexia</li> <li>Cardiac symptoms, hypotension, tachycardia arrhythmias</li> <li>Hepatotoxicity (jaundice)</li> <li>Hypersensitivity reactions e.g. pericarditis, pleuritis, myositis, vasculitis, ascites</li> <li>Lungs: nodular pulmonary shadows, hypoxaemia, cough, fever, chest pain</li> </ul>	<ul style="list-style-type: none"> <li>Avoid mixing in dextrose</li> <li>Incompatible with furosemide</li> <li>May exacerbate myocardial ischaemia or worsen ventricular ectopy</li> </ul>

contd...

Table 3.2: Antiarrhythmic drugs

Drug	Mechanism of action	Uses	Dose	Side effects	Remarks
<b>CLASS I</b>					
<b>BLOCK <math>Na^+</math> CHANNELS</b>					
<b>1A. Reduce <math>V_{max}</math> and prolong action potential duration</b>					
• Quinidine	—do—	VT and SVT; APC/VPC  PSVT, atrial fibrillation	200-300 mg 6-8 hr daily orally 400-600 mg every 2-3 hourly until reverted then 200-300 mg 6-8 hourly	<ul style="list-style-type: none"> <li>Hepatitis, cardiac toxicity</li> <li>Nausea, vomiting, diarrhoea</li> <li>abdominal pain, dizziness</li> <li>sweating, headache</li> <li>Haemolytic anaemia</li> <li>agranulocytosis, thrombocytopenic purpura</li> <li>Bradycardia, hypotension</li> <li>Allergy, rash, angioneurotic oedema, flushing</li> <li>Cinchonism, e.g. impaired hearing</li> </ul>	<ul style="list-style-type: none"> <li>Monitor for GI distress</li> <li>Monitor blood, liver, kidney functions</li> <li>Monitor ECG and serum levels</li> <li>Contraindications are acute infection, AV block, myocarditis, cardiac insufficiency, thrombocytopenia, prolong Q-T syndrome, myasthenia, digitalis toxicity, pregnancy</li> </ul>
• Procainamide	—do—	—do— Cardiac arrhythmias associated with anaesthesia, surgery	250-1000 mg every 3-6 hourly IM until oral therapy possible	<ul style="list-style-type: none"> <li>Same as above</li> <li>May induce lupus syndrome</li> </ul>	
<b>1. B. Do not reduce <math>V_{max}</math>, shorten action potential duration</b>					
• Mexiletine	—do—	Ventricular arrhythmias	200-400 mg tid upto upto 1200 mg/day/oral IV 200-250 mg IV infusion at a rate of 1 mg/min	<ul style="list-style-type: none"> <li>Nausea, vomiting, constipation</li> <li>Bradycardia, hypotension</li> <li>Confusion, convulsions</li> <li>ataxia and CNS disturbance</li> <li>Hepatitis, blood dyscrasias</li> </ul>	<ul style="list-style-type: none"> <li>Monitor ECG and BP</li> <li>Proarrhythmic drug may induce torsades de pointes</li> </ul>
• Phenytoin	—do—	<ul style="list-style-type: none"> <li>Digital induced ventricular arrhythmias</li> <li>As an antiepileptic</li> <li>For neuropathic pains e.g. trigeminal neuralgia, diabetic neuropathy</li> </ul>	Oral: 100 mg bid or tid IV: Dilantinisation 500-1000 mg as IV drip followed by 100 mg tid orally or IV	<ul style="list-style-type: none"> <li>Hepatitis, blood dyscrasias</li> <li>Read side effects in antiepileptic drugs</li> </ul>	<ul style="list-style-type: none"> <li>Read antiepileptics</li> </ul>
• Lidocaine	—do—	Ventricular arrhythmias	Loading dose: 1-1.5 mg/kg IV push, may be repeated as 0.5-1.5 mg/kg IV after 5-15 minutes followed by drip	<ul style="list-style-type: none"> <li>Nervousness, dizziness</li> <li>blurred vision, tremors</li> <li>numbness, tinnitus, nausea</li> <li>vomiting</li> <li>Bradycardia, hypotension</li> <li>cardiovascular collapse</li> </ul>	<ul style="list-style-type: none"> <li>BP monitoring and ECG control essential</li> <li>Bradycardia, AV blocks and cardiac decompensation are its contraindications</li> </ul>
					Contd...



Table contd..

Drug	Mechanism of action	Uses	Dose	Side effects	Remarks
<b>1. C</b>					
	<b>Reduce <math>V_{\max}</math> primarily, slow conduction and can prolong refractoriness</b>				
• Flecainide	—do—	Supraventricular and Ventricular arrhythmias	• 50-100 mg 12 hourly orally		• Monitor ECG
• Encainide	—do—	e.g. VT	• 25-50 mg 8 hourly orally		• May be proarrhythmic
• Propafenone	—do—		• 150 mg tid orally (upto 300 mg tid)		
<b>CLASS II BETABLOCKERS</b>					
<b>Read betablockers. They are discussed separately</b>					
<b>CLASS III DRUGS BLOCK <math>K^+</math> CHANNELS, BLOCK MULTIPLE PHASES OF ACTION POTENTIAL AND PROLONG REPOLARISATION</b>					
• Amiodarone	—do—	• Potentially life threatening ventricular arrhythmias unresponsive to conventional therapy	Oral: Loading dose 800 to 1600 mg/day for 1-3 weeks	• Liver toxicity • GI symptoms • Pulmonary fibrosis • Photosensitivity • Hypothyroidism or hyperthyroidism • Disorders of thyroid function e.g. hyper and hypothyroidism	• Monitor liver and thyroid function • Half life is 13-107 days • May be proarrhythmic
		• Supraventricular arrhythmias e.g. AV nodal, AV reentry, junctional tachycardia, atrial flutter and fibrillation	600-800 mg/day for 4 weeks then 400 mg/day <b>IV for VT:</b> 15 mg/min as infusion for 10 minutes followed by 1 mg/min for 6 hours for the next several days as necessary <b>VF:</b> 5 mg/kg I.V (diluted both 50-100 ml of 5% dextrose) push; if no response, then 10 mg/kg I.V push (diluted with 50-100 ml of dextrose) then maintain infusion at 1-2 mg/min (do not exceed 30-35 mg/kg/day)	• Cardiac toxicity e.g. bradycardia, ventricular tachyarrhythmias • Neuropathy	• Monitor ECG for bradycardia, prolongation of PR, QRS and QT <sub>c</sub> intervals • May increase serum levels of digoxin, class I drugs • High IV dose infusion may cause hypotension
• Bretylium tosylate	—do—	• Life-threatening ventricular arrhythmias unresponsive to conventional drugs • Drug-resistant ventricular tachyarrhythmias	<b>VF:</b> 5 mg/kg I.V (diluted both 50-100 ml of 5% dextrose) push; if no response, then 10 mg/kg I.V push (diluted with 50-100 ml of dextrose) then maintain infusion at 1-2 mg/min (do not exceed 30-35 mg/kg/day) Oral: 80 bid to 320 mg/day	• Orthostatic hypotension • Nausea, vomiting • Increased salivation and parotid pain	• Rapid IV infusion may cause hypotension • Avoid in digitalis toxicity
• Sotalol	Class II (betablocker) drug but has class III properties also	• Approved only to treat ventricular tachyarrhythmias		• Side effects of beta blockers may occur • Reduce the dose in	• Watch for proarrhythmic effect • Monitor QT interval, renal insufficiency

Contd...

Table contd..

Drug	Mechanism of action	Uses	Dose	Side effects	Remarks
<b>CLASS IV CALCIUM CHANNEL BLOCKERS—READ THE TEXT (DISCUSSED SEPARATELY)</b>					
<b>OTHER ANTIARRHYTHMICS</b>					
• Adenosine	<ul style="list-style-type: none"> <li>Slows conduction through AV node, interrupts reentry pathway in AV node</li> <li>Vasodilator</li> </ul>	<ul style="list-style-type: none"> <li>Narrow QRS complex paroxysmal supraventricular tachycardia (PSVT)</li> <li>Used for pharmacological stress testing</li> </ul>	IV: 6 mg IV push over 1-3 seconds (follow with 20 ml NS flush), if no response in 1-2 min; then 12 mg rapid IV push	<ul style="list-style-type: none"> <li>Flushing; dyspnoea, headache, chest pressure</li> <li>Hypotension</li> <li>Bradycardia and conduction disturbances</li> </ul>	<ul style="list-style-type: none"> <li>Can be used to determine origin of wide QRS tachycardia (ineffective in the presence of VT)</li> <li>Short half-life (&lt;5 sec)</li> <li>May produce transient bradycardia and ventricular ectopy</li> <li>Do not use in 2nd and 3 degree AV block or sick sinus syndrome unless pacemaker is <i>in situ</i></li> <li>May cause hypotension or asystole</li> </ul>
• Magnesium	<ul style="list-style-type: none"> <li>Hypomagnesaemia can precipitate dysarrhythmias and pump failure</li> <li>Electrolyte plays an important role in initiation and maintenance of cardiac muscle contraction</li> <li>Membrane stabilising agent and vasodilator</li> </ul>	<ul style="list-style-type: none"> <li>Refractory life-threatening arrhythmias (VT and VF) not responding to conventional drugs</li> <li>Torsade de pointes</li> <li>Post myocardial infarction arrhythmias</li> <li>Used for treatment of refractory epilepsy and bronchial asthma</li> </ul>	<b>For refractory VF/VT:</b> 1-2 g diluted in 100 ml 5% dextrose and infuse over 1-2 min <b>Post MI:</b> 1-2 g (8-16 mEq) in 50-100 ml in 5% dextrose and infuse over 5-60 minutes and follow 0.5-1.0 g/hr IV over 24 hr	<ul style="list-style-type: none"> <li>Flushing, headache, tachycardia, hypotension</li> </ul>	

rate, less prolongation of AV conduction. They have been shown to produce less depression of LV functions than betablockers without intrinsic sympathomimetic effect.

Only nonselective betablockers without intrinsic sympathomimetic activity have been demonstrated to reduce mortality in patients with myocardial infarction.

#### Actions

1. *Antihypertensive*: Both selective and nonselective betablockers antagonise the sympathetic effects on the heart, thus, lower cardiac output and arterial pressure. Metoprolol and atenolol, both cardioselective betablockers are preferred as antihypertensives.
2. *Antianginal effect*: Both cardioselective and non-selective betablockers are used in treatment of angina (stable, unstable and postmyocardial) because they reduce myocardial response to sympathetic stimulation and decrease myocardial O<sub>2</sub> demand.
3. *Antiarrhythmic effect*: All betablockers are classified class II antiarrhythmics except sotalol (has both class II and III effects). They are used in a variety of cardiac arrhythmias e.g. sinus tachycardia, anxiety neurosis with tachycardia, atrial flutter, atrial fibrillation, paroxysmal atrial tachycardia and ventricular arrhythmias. The antiarrhythmic effects is achieved by blockade of  $\beta_1$  receptors in the myocardium rather than quinidine like effect (some betablockers exert local anaesthetic and quinidine like effect). They delay conduction through AV node, hence, reduce heart rate response in atrial fibrillation or PSVT.
4. *Anti-thyroid*: Nonselective betablockers without intrinsic sympathomimetic activity are used to block the sympathetic stimulation in thyrotoxicosis, hence, are used for relief of thyrotoxic symptoms. In addition, they depress peripheral conversion of T<sub>4</sub> to T<sub>3</sub> and exert mild anti-thyroid effect.

*Uses of betablockers* They are used in the treatment of:

- Hypertension
- Angina
- Arrhythmias
- Some patients of CHF (e.g. carvedilol)
- Pheochromocytoma
- Mitral valve prolapse
- Anxiety neurosis

- Thyrotoxicosis
- Migrainous headache
- Essential tremors
- Glaucoma (timolol eye drops)
- Esmolol is the only betablocker used in the treatment of narrow QRS tachycardia (PSVT).

#### Drugs and Dosage

Atenolol	Oral: 25-150 mg daily
Metoprolol	25-450 mg in divided doses/day orally IV: Acute MI: 5 mg I.V push over 2 min × 3 doses then 50 mg orally every 6 hourly
Propranolol	Oral: 10-80 mg bid or qid upto 320 mg/day IV: 0.5-3.0 mg I.V push, may be repeated in 2 min then after every 4 hour
Nadolol	Oral: 40-120 mg/day upto 240 mg
Sotalol	Oral: 80 mg bid upto 320 mg/day
Timolol	Oral: 10-20 mg bid to max of 60 mg
Carvedilol	Oral: 3.75 to 12.5 mg/day
Esmolol	IV infusion: Loading dose 500 mg/kg over 1 minute followed by 50 mg/kg/min infusion over 4 min; may be repeated with increase in maintenance dose at interval of 5 min (do not exceed 200 mg/kg/min)

#### Adverse Effects

They are due to betablockade (Box 3.1).

**Box 3.1:** Adverse effects of betablockers

Cardiovascular	Noncardiovascular
<ul style="list-style-type: none"> <li>• Hypotension, bradycardia, AV blocks, precipitation of CHF, cold extremities,</li> <li>• Raynaud's phenomenon</li> </ul>	<ul style="list-style-type: none"> <li>• Bronchospasm</li> <li>• Hypoglycaemia</li> <li>• Allergic manifestations</li> <li>• Dizziness, insomnia, vivid dreams, depression, headache, muscle cramps</li> <li>• Nasal stuffiness, tiredness</li> <li>• Vomiting, diarrhoea, constipation</li> </ul>

**Contraindications**

- AV blocks
- Gross CHF refractory to digitalis
- Bronchial asthma or allergic conditions
- Cardiogenic shock
- Anaesthesia
- Oesophageal stricture and/or obstructive changes in GI tract

**Special precaution to be observed**

- Betablockers should not be stopped abruptly. They should be withdrawn slowly
- They should not be used in CHF unless patient is fully digitalised. Carvidolol and nebivolol are only used in CHF
- They should be avoided in combination with calcium channel blockers because of their potentiating effects
- Avoid their use in diabetes mellitus as they may mask features of hypoglycaemia, if it develops.
- When used I.V, give slowly or with atropine so to avoid severe bradycardia
- Pregnancy safety has not been proved

**Calcium Channel Blockers****Actions**

1. They block slow inward calcium current in all cardiac fibres including SA and AV nodes, thus, reduce the

height of action potential, shorten muscle action potential and prolong its duration, hence, are classified as class IV antiarrhythmic.

2. They depress the conduction through AV node. Pacemaker activity of SA node is also depressed.
3. They are vasodilators, hence, reduce the preload, for which they are used in CHF and HT.

**Indications**

(Table 3.3)

**Side effects and contraindications/special precaution**

See the Box 3.2.

**Classification**

The WHO has classified  $\text{Ca}^{++}$  antagonists according to their pharmacological and clinical effects.

**Class I (Verapamil) agents**, *in vivo*, they have most potent negative inotropic effect. Their depressant effect may precipitate CHF. They cannot be used with betablocker.

**Class II (Nifedipine, nicardipine, amlodipine)** agents do not depress conduction or contraction, therefore, the risk of precipitation of CHF is reduced. Therefore, they can be used in combination with betablockers as they even may reverse some of the negative inotropic effects of betablockers.

**Table 3.3:** Calcium channel blockers-indications, drug and dose

Indications	Drug	Route	Dosage
<ul style="list-style-type: none"> <li>• Antianginal, coronary spasm (prinzmetal's angina)</li> <li>• Hypertension</li> <li>• Non-Q wave MI (Non-ST elevation MI)</li> <li>• Control of ventricular rate in supraventricular tachycardia, atrial fibrillation and atrial flutter</li> <li>• Hypertrophic cardiomyopathy</li> <li>• Vasospastic phenomenon e.g. Raynaud's phenomenon</li> <li>• A combination of <math>\text{Ca}^{++}</math> antagonist (nifedipine, amlodipine) with nitrates form an effective combination for treatment of angina with heart failure, sick sinus syndrome or AV conduction disturbance</li> </ul>	Diltiazem:	Oral:	30-120 mg tid or qid
		IV:	0.25 mg/kg I.V push over 2 min; after 15 min 0.35 mg/kg I.V push over 2 minute
	Verapamil	Oral:	40-120 mg tid or qid
		IV	2.5-5 mg I.V push over 2 min after 15-30 min may repeat 5-10 mg I.V push over 2 min to a total of 20 mg
	Nifedipine	Oral:	10-40 mg tid or qid upto 160 mg/day
	Sublingual		5-10 mg SL to be repeated if necessary
	Amlodipine	Oral:	5-10 mg bid
Note: Nifedipine and amlodipine can only be combined with betablockers, otherwise combination of diltiazem and verapamil with betablockers is detrimental			

**Box 3.2: Calcium channel blockers**

Side effects	Contraindications
<ul style="list-style-type: none"> <li>• Dizziness, headache, flushes, fatigue, ankle oedema</li> <li>• Nausea, vomiting, constipation</li> <li>• Reflex tachycardia</li> <li>• Allergies</li> <li>• Gynaecomastia</li> <li>• Gingival hyperplasia</li> <li>• Reversible liver function impairment</li> <li>• IV administration may lead to decreased HR, (bradycardia), hypotension, depressed myocardial contractility, (CHF) Rarely 2nd and 3rd degree AV block</li> </ul>	<ul style="list-style-type: none"> <li>• Cardiogenic shock</li> <li>• 2nd and 3rd degree AV block</li> <li>• Severe bradycardia</li> <li>• Sick sinus syndrome</li> <li>• Uncompensated CHF</li> <li>• Severe LV dysfunction</li> <li>• Atrial flutter or fibrillation with accessory bypass</li> </ul>
<b>Drug Interactions:</b> Digoxin, betablockers, anti-arrhythmics, theophylline, carbamazepine, phenytoin, rifampicin etc.	<b>Precautions</b> <ul style="list-style-type: none"> <li>• Pregnancy, lactation</li> <li>• Poor cardiac reserve</li> <li>• First degree AV block, bradycardia, conduction disturbances</li> <li>• Acute phase of MI</li> <li>• Concomitant use of betablockers</li> <li>• Hepatic and renal impairment</li> </ul>

**Class III agents (e.g. diltiazem).** It has a little or negligible negative inotropic effect. It has a selective effect on coronary arteries with little effect on peripheral vessels, hence, does not cause reflex tachycardia.

**ANTIHYPERTENSIVES**

Drugs used in the treatment of hypertension according to site of action are tabulated (Table 3.4).

- a. Diuretics—Read diuretics
- b. Anti-adrenergic
  - i. Central acting e.g. clonidine, methyl dopa
  - ii. Autonomic ganglia e.g. trimethaphan
  - iii. Nerve endings e.g. reserpine, guanethidine
  - iv. Alpha blockers e.g. phentolamine, phenoxybenzamine, prazosin
  - v. Betablockers
  - vi. Alpha/betablockers e.g. labetalol
- c. Vasodilators: Vascular smooth muscle relaxants e.g. hydralazine, minoxidil, diazoxide, nitroprusside
- d. Angiotensin converting enzyme inhibitors (ACE inhibitors): They include; captopril, enalapril, benazepril, fosinopril, lisinopril and ramipril

- e. Angiotensin receptors blockers: They include losartan, irbesartan, candesartan
- f. Calcium channel blockers: They include, nifedipine, amlodipine, felodipine, nicardipine, diltiazem, verapamil

**Choice of Antihypertensive During Pregnancy**

The safety of antihypertensive during pregnancy is depicted in Table 3.5.

**Hypertension in Elderly**

Antihypertensive therapy reduces the incidence of cardiovascular complications. This benefit is evident upto 85 years of age. The criteria for treatment include diastolic blood pressure  $\geq 100$  mm Hg or systolic  $\geq 160$  mm Hg over 3 to 6 months observation. A low dose of thiazide is the first drug of choice with addition of a betablocker when required.

**Antihypertensive drug choices in specific situations**

Table 3.6.

**ANTIANGINAL DRUGS**

Angina can be stable (due to atheromatous plaques in the coronary artery) or unstable (due to plaque rupture) It is important to differentiate between the two. The anti-anginal drugs include;

1. Nitrates
2. Betablockers (already discussed)
3. Calcium channel blockers (already discussed)
4. Potassium channel activators

Most patients of angina pectoris are usually treated with betablockers or calcium channel blockers. However, short-acting nitrates can play an important role both as prophylactic (drug to be taken before exertion) and during acute chest pain occurring at rest or exertion. Nitrates are also used as sole therapy in elderly patients with infrequent attacks.

**Nitrates****Actions**

1. Their precise mechanism of action is unknown but appears to depend on their conversion to the nitrate



Table 3.4: Antihypertensive drugs

Site of action	Drug	Dosage	Indications	Contraindication/cautions	Common side effects
Diuretics	Have been discussed separately				
<b>Antiadrenergic Drugs</b>					
Central	Clonidine	Oral: 0.05-0.6 mg twice daily	<ul style="list-style-type: none"> <li>Mild to moderate hypertension</li> <li>Hypertension with renal disease</li> </ul>	—	Postural hypotension, sedation, dry mouth, impotence, constipation, fluid retention, depression, sleep disturbance, rebound hypertension after abrupt withdrawal
	Methyldopa (also acts by blocking sympathetic nerves)	Oral: 250-1000 mg twice daily I.V: 250-1000 mg 4-6 hourly	<ul style="list-style-type: none"> <li>Mild to moderate hypertension</li> <li>Drug of choice for hypertension in pregnancy</li> <li>Intravenously used for malignant hypertension</li> </ul>	<ul style="list-style-type: none"> <li>Phaeochromocytoma</li> <li>Hepatic disease</li> <li>During MAO inhibitor treatment</li> </ul>	Postural hypotension, sedation, fatigue, diarrhoea, impaired ejaculation, fever, gynaecomastia, lactation, positive Coomb's test, chronic hepatitis, ulcerative colitis, SLE like syndrome
Autonomic ganglia blocker	Trimethaphan	I.V: 1-6 mg/min	Severe and malignant hypertension	Severe coronary artery disease, severe cerebrovascular insufficiency, diabetes on hypoglycaemic therapy, glaucoma, prostatism	Postural hypotension, visual symptoms, dry mouth, constipation, urinary retention, impotence
Nerve endings, e.g. Adrenolytic	Reserpine	Oral: 0.05-0.25 mg daily	<ul style="list-style-type: none"> <li>Mild to moderate hypertension in young</li> <li>Raynaud's phenomenon</li> </ul>	Phaeochromocytoma, peptic ulcer, depression, MAO inhibitor therapy	Depression, nightmares, nasal congestion, dyspepsia, diarrhoea, impotence
	Guanethidine	Oral: 10-15 mg/day	Moderate to severe hypertension	Phaeochromocytoma, coronary artery disease, cerebrovascular insufficiency, MAO inhibitor therapy	Postural hypotension, bradycardia, dry mouth, diarrhoea, impaired ejaculation, oedema, asthma
	Phentolamine	Oral: 1-5 mg bolus	Suspected or proved phaeochromocytoma	Severe coronary artery disease	Tachycardia, weakness, dizziness, flushing
Alpha receptors blocker	Phenoxybenzamine	Oral: 10-50 mg once or twice a day	Proved phaeochromocytoma	—	Postural hypotension, miosis, tachycardia, dry mouth, nasal congestion
	Prazosin	Oral: 1-10 mg twice a day	<ul style="list-style-type: none"> <li>Mild to moderate hypertension</li> <li>Raynaud's phenomenon</li> </ul>	Use with caution in elderly	Sudden syncope, headache, sedation, dizziness, tachycardia, dry mouth, fluid retention
<b>Betablockers</b>	Read as already discussed				
<b>Alpha and Beta receptor blocker</b>	Labetalol	Oral: 100-600 mg twice a day; I.V: 2 mg/min	Similar	Similar	Similar to betablockers with more postural effects

Contd...

Table contd..

Site of action	Drug	Dosage	Indications	Contraindication/cautions	Common side effects
<b>Vasodilators</b>					
Vascular smooth muscle	Hydralazine	Oral: 10-75 mg 4 times a day	As an adjuvant to treatment of moderate to severe hypertension	Lupus erythematosus (SLE), severe coronary artery disease	Headache, tachycardia, angina, nausea, anorexia, vomiting, diarrhoea, SLE syndrome, rash, oedema
	Minoxidil	Oral: 2.5-40 mg twice a day	Severe hypertension	Severe coronary artery disease	Tachycardia, aggravation of angina, fluid retention, hair growth (hypertrichosis), coarsening of facial features, pericardial effusion
	Diazoxide	IV 1-3 mg/kg upto 150 mg rapidly	Severe to malignant hypertension	Diabetes, hyperuricaemia, CHF	Hyperglycaemia, hyperuricaemia, fluid retention, apprehension, weakness, nausea, vomiting,
	Nitroprusside	IV: 0.5-8 (mg/kg/min)	Malignant hypertension		diaphoresis, muscle twitching, cyanide toxicity
<b>Calcium Channel Blockers</b>					
Read as already discussed					
<b>Angiotensin Converting Enzyme (ACE) Inhibitors</b>					
The drugs by blocking the ACE, suppress the angiotensin II formation, thus, affect primarily renin-angiotensin aldosterone system	Captopril	Oral: 12.5-75 mg twice a day	<ul style="list-style-type: none"> <li>Mild to moderate hypertension</li> <li>Renal artery stenosis (unilateral)</li> <li>CHF refractory to digoxin and diuretics</li> <li>Hypertension with renal failure (S. creatinine &lt; 3.5 mg%)</li> <li>Nephrotic syndrome to reduce albuminuria</li> </ul>	<ul style="list-style-type: none"> <li>Renal failure (reduce the dose)</li> <li>Bilateral renal artery stenosis</li> <li>Pregnancy</li> </ul>	Leucopenia, pancytopenia, hypotension, angioedema, cough, urticarial rash, fever, loss of taste, acute renal failure in bilateral renal artery stenosis, hyperkalaemia
	Enalapril	Oral: 2.5-40 mg/day			Same as captopril, but cough and angioedema can be more frequent. All are given once daily dose but side-effects are reduced if given twice a day
	Benazepril	Oral: 10-40 mg/day			
	Fosinopril	Oral: 10-40 mg/day			
	Lisinopril	Oral: 5-40 mg/day			
	Ramipril	Oral: 2.5-20 mg/day			
	Perindopril	Oral: 2-4 mg/day			
<b>Angiotensin Receptor Blockers (ARBs)</b>					
They block angiotensin receptors	Losarten	Oral: 25-50 mg once or twice/day	<ul style="list-style-type: none"> <li>Mild to moderate hypertension</li> <li>Renal hypertension</li> <li>Diabetic nephropathy with hypertension</li> </ul>	<ul style="list-style-type: none"> <li>Pregnancy</li> <li>Bilateral renal artery stenosis</li> </ul>	<ul style="list-style-type: none"> <li>Hypotension, acute renal failure in bilateral renal artery stenosis, hyperkalaemia</li> </ul>
	Irbesarten	Oral: 150-300 mg once or twice/day			

Note: Previously adopted step-ladder pattern of treatment for hypertension is obsolete now-a-days. The drug is chosen depending on the situation. Initially, monotherapy is instituted in all grades of hypertension, substituted by polytherapy depending on the severity of hypertension, specific situation and response to treatment. Diuretics and betablockers/calcium channel blockers are preferred for initial therapy.

**Table 3.5:** Safety of antihypertensive during pregnancy

<i>Class of drug</i>	<i>Safety</i>	<i>Recommendation</i>
Methyldopa Betablockers	Safe Limited experience in first trimester. Use in late pregnancy can cause neonatal hypoglycaemia and bradycardia	Treatment of choice Avoid in first trimester, if possible
Calcium channel blockers Diuretics	Limited experience Theoretical risk of compromising uteroplacental blood flow	Second-line treatment Avoid
ACE inhibitors	Serious problems in the fetus may occur such as oligohydramnios and renal dysfunction, especially after exposure in 2nd and 3rd trimester	Contraindicated
<i>Note:</i> 1. In the second and third trimester, antihypertensive agents are not indicated unless the diastolic pressure exceeds 95 mm of Hg. 2. Hypertensive female becoming pregnant and pregnancy with hypertension (pregnancy-induced hypertension, eclampsia, pre-eclampsia) are different terms but treatment remains same.		

**Table 3.6:** Choice of antihypertensive in specific conditions

<i>Condition</i>	<i>Preferred</i>	<i>Alternative/Avoid</i>
Diabetes Mellitus	<ul style="list-style-type: none"> <li>• ACE-inhibitor</li> <li>• ARB (angiotensin receptor blocker)</li> <li>• Calcium antagonist</li> </ul>	<ul style="list-style-type: none"> <li>• Avoid thiazide diuretic</li> <li>• Avoid betablockers</li> </ul>
Hyperlipidaemia	$\alpha_1$ -antagonist	<ul style="list-style-type: none"> <li>• ACE inhibitor</li> <li>• Calcium antagonist</li> <li>• Avoid diuretic and betablockers</li> </ul>
Angina	<ul style="list-style-type: none"> <li>• Betablockers</li> <li>• Calcium antagonist</li> </ul>	
Heart failure	ACE inhibitor	Diuretics and $\alpha_1$ -antagonists
Asthma	—do—	Avoid betablockers
Peripheral vascular disease	Calcium antagonist	$\alpha_1$ -antagonist, Avoid betablockers
Elderly patients	Low dose thiazide and/or a calcium channel blocker	

ion which is considered to generate oxide. This is possibly the same molecule as “endothelial derived relaxation factor (EDRF), the endogenous nitrate” responsible for vasodilation in hypoxia. Therefore, the predominant effect of nitrates is vasodilation of the venous capacitance vessels (reduction of preload on the heart). This reduction of preload reduces the pressure in the ventricles which, in turn, reduces wall tension, hence, reduces myocardial  $O_2$  demand. They also dilate arteriolar vessels, thus, also reduce afterload on the heart with the result the amount of work of the heart is reduced.

2. In addition, they may increase coronary blood flow (a little effect), but they appear to redistribute blood to ischaemic areas particularly the subendocardial regions which are subject to the greatest amount of pressure during systole.

By both these actions, they relieve angina both exertional and vasospastic.

#### Uses

1. Prophylaxis and treatment of angina. They are used in exertional angina and to relieve coronary spasm in Prinzmetal angina (rest angina).

**Table 3.7:** Commonly used nitrates

Drug	Usual dose	Side effects	Contraindications
1. Sublingual nitroglycerine	0.3-0.6 mg	Headache, flushing, dizziness, tachycardia, hypotension	Intolerance or side effects
2. Isosorbide dinitrate (short-acting)	80-120 mg	Flushing, headache dizziness, tachycardia, GI upset and sleep disturbance, methaemoglobinaemia, cyanosis	As above. There may be worsening of ischaemia on withdrawal
3. Transdermal nitroglycerine (skin patch)	0.4-1.2 mg/hr for 12-24 hr	Same as above	Same as above
4. Isosorbide-5 mononitrate (long-acting)	20-30 mg bid or 40 mg od	Same as above	Same as above

- Being smooth muscle relaxant, they find a place in the treatment of gastrooesophageal spasms and nutcracker oesophagus.
- Intravenous nitrates can be used in unstable angina, acute myocardial infarction with or without left heart failure, to control blood pressure in pre-operative hypertension and treatment of malignant hypertension. They can be used for control of hypertension during surgery.
- Being, venodilators they reduce portal venous pressure, may, sometimes be useful for treatment of acute variceal bleed due to portal hypertension.
- Nitrates with calcium channel blockers can be used for treatment of angina with CHF, sick sinus syndrome and conduction disturbance.

*Drug dosage and route of administration (Table 3.7).*

### Potassium Channel Activator (Nicorandil)

Nicorandil belongs to a new class of antianginal agents called *potassium channel activators*. It causes veno-arteriolar dilatation. It acts by increasing membrane conductance to K<sup>+</sup> ions which causes hyperpolarisation of vascular smooth muscle membrane, thus reducing their excitability and leading to arteriolar dilatation. Unlike, nitrates, tolerance does not develop to nicorandil-an added advantage over nitrates. Being both venous and arteriolar dilator, it increases coronary blood flow and perfusion of poststenotic regions of the myocardium without causing a “coronary steal-syndrome” and restores

the balance between O<sub>2</sub> supply and demand of the myocardium and thereby relieving angina. It does not affect HR or BP in patients with angina.

#### Uses

It is used either as a monotherapy or in combination with other antianginal drugs.

#### Side-effects

Headache, vasodilation, vomiting, dizziness, asthenia, hypotension, and/or tachycardia at high rates.

### ANTIPLATELET AGENTS

These drugs inhibit platelet functions (adhesion and aggregation) and play a role in the management of patients with arterial vascular disease and thromboembolism. Commonly used drugs and their dosage, side effects are given in Table 3.8. These drugs include:

- Inhibitor of platelet cyclo-oxygenase activity, e.g. aspirin, dipyridamole
- Inhibitor of ADP-induced platelet aggregation, e.g. ticlodipine and clopidogrel.

#### Indications and Contraindications (Box 3.3)

They are used in variety of conditions either alone or in combination with anticoagulants for reduction of frequency of transient ischaemic attacks in patients with CVA and progression of unstable angina to myocardial infarction.

**Table 3.8:** Commonly used antiplatelet agents

Drug	Action	Dose	Side effects
Aspirin	Irreversibly inactivates the enzyme cyclo-oxygenase and thereby inhibit platelet production of thromboxane A <sub>2</sub>	150-300 mg as a single dose in a day	<ul style="list-style-type: none"> <li>It may cause allergic or asthmatic reactions, GI intolerance</li> </ul>
Ticlopidine	Inhibits ADP-induced platelet aggregation	250 mg twice daily with food	<ul style="list-style-type: none"> <li>GI symptoms (e.g. nausea, vomiting, abdominal pain, diarrhoea)</li> <li>Skin rashes</li> <li>Neutropenia, GI haemorrhage</li> <li>Headache, tinnitus</li> </ul>
Clopidogrel	Inhibits ADP-induced platelet aggregation	300 mg as a loading dose followed by 75 mg once daily	<ul style="list-style-type: none"> <li>Neutropenia, haemorrhage, agranulocytosis</li> <li>Skin rash</li> <li>GI symptoms e.g. nausea, dyspepsia, gastritis, constipation</li> </ul>
A combination of aspirin and clopidogrel	Over all inhibition of platelets aggregation	Aspirin and clopidogrel in usual dosage	<ul style="list-style-type: none"> <li>Thrombotic thrombocytopenic purpura</li> </ul>

**Box 3.3:** Indications and contraindications for antiplatelet therapy

Indications	Contraindication
<b>1. Cardiovascular</b> <ul style="list-style-type: none"> <li>Unstable angina pectoris</li> <li>Primary prevention of myocardial infarction</li> <li>Secondary prevention of MI</li> <li>Following coronary by-pass grafting</li> <li>Following insertion of a stent or prosthetic valve</li> </ul>	<ul style="list-style-type: none"> <li>Peptic ulcer</li> <li>Haemophilia</li> <li>Bleeding disorders</li> <li>Lactation</li> <li>Haemodialysis patients</li> <li>Active bleeding</li> </ul>
<b>2. Cerebrovascular</b> <ul style="list-style-type: none"> <li>Treatment ischaemic stroke, completed stroke</li> <li>Secondary prevention of CVA</li> </ul>	
<b>3. Renal disease</b> <ul style="list-style-type: none"> <li>To maintain the patency of AV cannula</li> <li>To slow the progression of glomerular disease</li> </ul>	
<b>4. Miscellaneous</b> <ul style="list-style-type: none"> <li>Peripheral vascular disease</li> <li>Prevention of micro and macrovascular complications of type 2 diabetes</li> </ul>	

## ANTICOAGULANTS

These agents retard fibrin deposition on established thrombi and prevent the formation of new thrombi. The drugs include;

1. Heparin—for acute or immediate anticoagulation as well as for long-term administration.
2. Oral anticoagulants—for chronic or long-term anticoagulation.

### Indications

1. Acute venous thrombosis and pulmonary embolism.
2. Chronic oral anticoagulation is used to prevent cerebral arterial embolism from cardiac sources such as ventricular mural thrombi, atrial thrombi, or prosthetic valve thrombi or thrombi from an atherosclerotic, partially occluded or stenosed carotid or vertebral artery.
3. They are used, less successfully, to treat peripheral or mesenteric arterial thrombosis and dural sinus thrombosis.

### Acute Anticoagulation with Heparin

**Action** Heparin acts as an anticoagulant by inhibiting a number of activated factors (thrombin, XIIa, XIa, Xa,



IXa, VIIa) and binds to and activate antithrombin III. It is an extremely potent anticoagulant that can dramatically reduce thrombin generation and fibrin formation in patients with acute venous and arterial thrombosis and embolism. It is given as IV infusion at a rate sufficient to raise the activated partial thromboplastin time (APTT) or INR to 2-2.5 times the patient's preheparin APTT/INR. This requires infusion of approximately 1000 USP units/hour and is continued for 2-3 days while patients are begun on oral anticoagulants simultaneously to achieve appropriate prolongation of prothrombin time during shifting period.

Alternative to continuous IV infusion, heparin can be administered as 5000 units four times a day either subcutaneously or intravenously.

#### Types of heparin

1. Unfractionated
2. Low-molecular weight heparin

The low molecular weight heparin has many advantages over unfractionated heparin;

- i. The low molecular weight heparin can be administered subcutaneously once or twice daily
- ii. Their pharmacokinetics are so predictable that APTT monitoring is not, required.

- iii. The low-molecular weight heparin is less immunogenic, hence, less likely to cause thrombocytopenia
- iv. Low molecular weight heparin can be given to outpatients

#### Indication for anticoagulation with heparin

Heparin anticoagulation is the treatment of choice for acute venous thrombosis. The indications, dose and route of administration of heparin are given in Table 3.9.

#### Chronic Oral Anticoagulation

The oral anticoagulants include two groups

1. Coumarins e.g. warfarin and dicumarol
2. Indandiones e.g. phenindione

#### Actions

Both these groups of drugs reduce the activity of vitamin K dependent clotting factors (prothrombin, VII, IX and X) by interfering with their synthesis in the liver. Their effect does not become apparent until the body's existing supplies of vitamin K dependent factors has been exhausted, that is why, they take 2-3 days for the anticoagulant effect to develop fully. Similarly on withdrawal, the anticoagulant activity will not disappear

**Table 3.9:** Anticoagulant therapy with heparin

Indications	Dose (USP units)	Route of administration
1. Prophylaxis in general surgery	5000 q 12 hr	Subcutaneous
2. Prophylaxis in medical conditions such as patients with CHF, cardiomyopathy or myocardial infarction	10,000 q 12 h	Subcutaneous
3. Treatment of unstable angina and non-ST elevation myocardial infarction (NSTEMI)	5000 as bolus then 1000 q per hour	Intravenous
4. Acute pulmonary embolism (venous thromboembolism)	5,000 as bolus then 1000 q per hour	Intravenous
5. Venous thromboembolism (prophylaxis in pregnancy, warfarin failure or chronic disseminated intravascular coagulation)	1000 q per hour	Subcutaneous pump
6. Haemodialysis	5000 as bolus then further 5000 if session of dialysis exceeds 4 hr	I.V into arterial line of circuit prior to session of dialysis
Low molecular heparin (Flaxaprin, enoxaprin)		
1. Prophylaxis in general surgery:	Flaxaprin 3200 U or enoxaprin 2000 U (20 mg) deep subcutaneous 2 hour before surgery then daily for 7-10 days	
2. Deep vein thrombosis:	Flaxaprin 6400/day for 5-7 days or Enoxaprin 1-1.5 mg/kg/day until oral anticoagulation is achieved	
3. Haemodialysis:	Enoxaprin 1 mg/kg into arterial line of circuit prior to dialysis then 0.5-1 mg/kg may be given again if session exceeds 4 hrs of dialysis	

**Table 3.10:** Oral anticoagulants

Drug	Dose	Indications	Effective anticoagulation
Warfarin	5-10 mg/day then titrate the dose to achieve effective anticoagulation	<ul style="list-style-type: none"> <li>Treatment, prevention and recurrence of deep vein thrombosis and pulmonary or cerebral embolism</li> </ul>	<p>Effective anticoagulation means the prolongation of prothrombin time (PT) of the patient by 1.5 to 2 times than the control. The International Normalised Ratio (INR) or PTI (%) is the well recognised method for effective anticoagulation which is calculated as follows</p> $\text{INR} = \frac{(\text{PT of the patient})}{\text{Normal PT}}$ $\text{PTI (\%)} = \frac{\text{PT of patient}}{\text{Normal PT}} \times 100$ <p>Note: The intensity of anticoagulation to be achieved depends on the INR or PTI (%) and varies with clinical conditions from 1.5 to 4 times</p>
Dicoumarol	8-12 mg 1st day, 4-8 mg 2nd day, maintenance dose 1-8 mg/day so as to achieve effective anticoagulation	<ul style="list-style-type: none"> <li>Prophylaxis for left atrial or ventricular thrombi</li> <li>Prophylactic therapy for paroxysmal atrial fibrillation or prosthetic valve</li> <li>Patients with lupus anticoagulants and risk of thromboembolism</li> <li>Patients with chronic indwelling venous catheter to prevent clot formation at the catheter tip</li> </ul>	

**Table 3.11:** Side effects and contraindication of anticoagulants

Drug	Contraindication	Side effects
Heparin	<ul style="list-style-type: none"> <li>Haemorrhagic conditions</li> <li>Bleeding tendencies</li> <li>Severe liver or kidney disease</li> <li>Uncontrolled hypertension</li> </ul>	<ul style="list-style-type: none"> <li>Haemorrhage is common</li> <li>Hypersensitivity reactions</li> <li>Thrombocytopenia</li> <li>Alopecia</li> </ul>
Oral coumarine derivative	<ul style="list-style-type: none"> <li>Pre-existing tendency to haemorrhage e.g. peptic ulcer, cerebrovascular haemorrhage</li> <li>Severe hepatic or renal disease</li> <li>Pregnancy</li> </ul> <p><i>Special precautions</i></p> <ul style="list-style-type: none"> <li>Antibiotics</li> <li>Fat malabsorption</li> <li>Sensitivity to these drugs is increased by aspirin, indomethacin, methyldopa, clofibrate</li> <li>Sensitivity is decreased by barbiturates, rifampicin, haloperidol, hence, if therapy with these drug is stopped, anticoagulant effect may be increased. Therefore, careful control of dosage with careful and frequent monitoring of PT is essential</li> </ul>	<ul style="list-style-type: none"> <li>Osteoporosis on prolonged use</li> <li>Haemorrhage</li> <li>Dermatitis</li> <li>Fever</li> <li>Nausea, diarrhoea</li> <li>A painful purple discolouration of toes and skin necrosis</li> </ul>

until the liver has once again produced these factors. As discussed earlier, patient should remain on heparin until the appropriate dose of oral anticoagulant is achieved.

- Dose and indications of oral anticoagulants (Table 3.10)
- Side effects and contraindications of anticoagulants (Table 3.11).

**FIBRINOLYTIC OR THROMBOLYTIC AGENTS**

Fibrinolysis is an important part of normal haemostatic process, is initiated by the release of tissue plasminogen activator (tPA) or pro-urokinase (Pro UK) from endothelial cells. The fibrinolytic drugs actually accelerate the process of fibrinolysis by preferentially activating plasminogen which, is adsorbed on to fibrin clot, is converted into plasmin (proteolytic enzyme) which lyses the fibrin clot or thrombus to achieve thrombolysis or fibrinolysis.

*Drugs*

The pharmacologic agents being used to accelerate clot dissolution are either derived from natural products or are chemically modified derivatives. They differ with respect to fibrin specificity and some types of complications. For example, some patients have antistreptococcal antibodies in the blood that may react with streptokinase and reduce its potency and cause immunogenic or fibrile reaction. Similarly streptokinase can only be used once or twice for this purpose because antibodies are formed against it after its first use.

*Indications, Dosage, Side Effects*

Table 3.12.

*Parameters of Fibrinolysis*

- Fall in fibrinogen level
- Prolongation of the thrombin time and euglobulin lysis time

*Precautions During Streptokinase Therapy*

Some patients may develop acute allergic symptoms including urticaria and occasionally serum sickness reactions. The corticosteroids and antihistaminics should be at the bedside for such an event. However, some physicians use concomitant use of corticosteroids and an antihistaminic agent to avoid such reaction. Blood pressure, pulse and ECG should be continuously monitored.

*Success of Coronary Thrombolysis in Acute MI*

The thrombolysis should be attempted as early as possible within first 6 hrs when clot is fibrinous (fresh). Delayed use of streptokinase may make it unsuccessful.

The parameters of successful thrombolysis are;

1. Relief of pain or cardiac symptoms.
2. Return of elevated ST segment to normal or near normal level or reduction in ST elevation by >50%
3. Reperfusion arrhythmias e.g. nodal ectopics, idionodal rhythm or first degree AV block.

**Table 3.12:** Fibrinolytic agents

Agent	Indications	Dose	Adverse effects
1. Recombinant tissue plasminogen activator (rt PA) (Source-recombinant)	Lysis of coronary arterial thrombi in acute MI	<ul style="list-style-type: none"> <li>• 100 mg IV over 3 hours in hospital only</li> <li>• Current regimen is 15 mg bolus followed by 50 mg IV over 30 min then rest 35 mg over one hour</li> </ul>	Localised bleeding, intracerebral haemorrhage, bleeding into GI and urinary tract. Nausea, vomiting, headache, rash, pruritus
2. Urokinase (UK) (source: renal tubular cell cultures)	<ul style="list-style-type: none"> <li>• Thrombolysis in acute MI, deep vein thrombosis, peripheral arterial occlusion</li> </ul>	4400 I.U/ kg over 10-30 min IV	<ul style="list-style-type: none"> <li>• Bleeding (localised or intracerebral or GI tract) nausea and vomiting</li> </ul>
3. Streptokinase (source: $\beta$ -haemolytic streptococci)	<ul style="list-style-type: none"> <li>• Clot lysis in acute MI</li> <li>• Acute thrombosis of arteries</li> <li>• Pulmonary embolism</li> <li>• Deep vein thrombosis</li> <li>• Veno-occlusive disease of liver</li> </ul>	<p><b>For acute MI:</b> 750,000-1.5 million IU over one hour</p> <p><b>For Deep vein thrombosis</b> 1.5 million IU over 6 hours</p>	<ul style="list-style-type: none"> <li>• Haemorrhage, hypotension, arrhythmias, febrile reactions, anaphylaxis (rare) pulmonary oedema, nausea, vomiting</li> </ul>

Note: Heparin should be started at the same time as an fibrinolytic agent and continued for 7-10 days.

## DIURETICS

### Definition

These are the drugs which produce natriuresis with obligatory loss of water.

### Indications

They are used in following conditions;

1. Congestive heart failure due to any cause
2. Cirrhosis of liver with oedema
3. Nephrotic syndrome (nephrotic oedema)
4. Hypoproteinaemia with edematous state
5. Treatment of hypertension
6. Toxaemia of pregnancy
7. Forced diuresis for dialysable poison (salicylates, barbiturate) and hypercalcaemia

All diuretics are effective in eliminating oedematous states, but the selection of diuretics is more difficult, and abnormality in serum electrolytes must be taken into account. Overtreatment must be avoided, since, resultant hypovolemia may reduce cardiac output, interfere with renal functions and produce profound weakness and lethargy.

Because of different sites of actions they can be used in combinations. They can be used as an adjunct to appropriate therapy directed against the cause of the disease with oedema such as these can be combined with digoxin, antihypertensives and so on. They potentiate digitalis toxicity due to hypokalaemia.

The hypokalaemia is a dangerous side effect of potent loop diuretic e.g. furosemide, hence, a  $K^+$  sparing diuretic may be combined, but, this combination becomes again dangerous in hyperkalaemia associated with oedematous state i.e. renal failure.

### Commonly Used Diuretics

#### Thiazides and Related Diuretics

**Actions:** They induce diuresis by inhibiting selective renal tubular reabsorption of sodium and chloride chiefly in the early distal tubule (cortical diluting segment). Some also exhibit weak carbonic anhydrase inhibiting activity. All diuretics increase renal excretion of sodium and chloride in approximately equal amounts (Table 3.13).

#### Loop Diuretics

The loop diuretics are physiologically similar but differ chemically. They are most potent diuretics and remain effective despite the elimination of extracellular fluid volume where other diuretics lose their effectiveness. These drugs are effective orally and intravenously. Due to their effectiveness, they are useful in all emergency oedematous states, particularly in refractory heart failure and pulmonary oedema. These are even effective in patients with hyponatraemia, hypoalbuminaemia, hypochloraemia, hypokalaemia and reductions in GFR and to produce a diuresis in patients in whom thiazide diuretics and aldosterone antagonists, alone or in combination are ineffective. In refractory heart failure, the action of loop diuretics may be potentiated by intravenous administration and the addition of other diuretics.

#### Actions

They reversibly inhibit the reabsorption of  $Na^+$ ,  $K^+$ ,  $Cl^-$  in the thick ascending limb of *Henle's loop*. They may also induce renal cortical vasodilation and can produce rates of urine formation that may be as high as one-fourth of GFR (glomerular filtration rate).

#### Commonly used loop diuretics (Table 3.14)

This group includes bumetanide, furosemide, torsemide and ethacrynic acid

#### Potassium-sparing diuretics

This group includes;

1. Aldosterone antagonists-spirolactone
2. Triamterene and amiloride

#### Actions

Spirolactone competitively inhibits the distal tubular reabsorption of sodium and excretion of potassium by antagonising the action of aldosterone on the distal tubules. Thus, diuresis occurs with excretion of sodium and retention of potassium hence called *potassium sparing effect*. Its specific indication is to produce diuresis where oedematous state is associated with hyperaldosteronism, i.e. cirrhosis of liver, CHF and nephrotic syndrome.

**Table 3.13:** Commonly used thiazide diuretics and similar compounds

Drug	Dose	Contraindications/caution	Frequent side effects
Hydrochlorthiazide	Oral: 12.5-25 mg daily or twice daily	Anuria, hepatic coma, concomitant lithium therapy, diabetes mellitus, hyperuricaemia, primary hyperaldosteronism and hypersensitivity to thiazides	<ul style="list-style-type: none"> <li>• <b>GI symptoms:</b> nausea, vomiting, anorexia</li> <li>• <b>CNS:</b> headache, dizziness, paraesthesias</li> <li>• <b>Blood</b>—blood dyscrasias</li> <li>• <b>Metabolic:</b> hyperglycaemia, hyperuricaemia, hypercalcaemia, hypokalaemia</li> <li>• <b>CVS:</b> orthostatic hypotension</li> <li>• <b>Skin:</b> photosensitivity, rash</li> </ul>
Note: K <sup>+</sup> supplementation must be made with their use			
Chlorthalidone (not thiazide, but has similar action)	50-100 mg orally on alternate days as single dose	Severe renal failure, pregnancy, lactation, diabetes, gout	<ul style="list-style-type: none"> <li>• GI symptoms</li> <li>• Cardiac arrhythmias</li> <li>• Hypokalaemia, hypomagnesaemia</li> <li>• Photosensitivity, rash</li> <li>• Blood dyscrasias</li> <li>• Postural hypotension, fatigue, weakness</li> <li>• Impotence</li> <li>• Rarely jaundice</li> <li>• Hypokalaemia</li> <li>• GI symptoms</li> <li>• Fatigue weakness</li> <li>• Photosensitivity, rash</li> </ul>
Metolazone (Quinethazine derivative having similar action to thiazide but is not a thiazide)	5-10 mg/day orally as a single dose	Pregnancy, lactation, diabetes, gout,	<ul style="list-style-type: none"> <li>• GI symptoms</li> <li>• Fatigue weakness</li> <li>• Photosensitivity, rash</li> </ul>
Note: Metolazone has been reported to be effective in the presence of moderate renal failure			

**Table 3.14:** Commonly used loop diuretics

Drug	Dosage	Contraindication/caution	Side-effects	Comment
Furosemide	Oral: 20-80 mg as a single dose or divided IV 20-80 mg or IM or slow IV daily or as required Children 1 mg/kg body wt. daily (max 20 mg/day) orally or IV	<ul style="list-style-type: none"> <li>• Hepatic coma,</li> <li>• Hypovolemia, hypotension</li> <li>• Hyponatremia, hypokalaemia</li> <li>• Addison's disease</li> <li>• Caution in patients with diabetes, gout, pregnancy, lactation</li> </ul>	<ul style="list-style-type: none"> <li>• GI upset, malaise</li> <li>• Rash</li> <li>• Deafness</li> <li>• Gout</li> <li>• Blood dyscrasias</li> <li>• Hypokalaemia</li> <li>• Hyperglycaemia</li> <li>• Hypocalcaemia</li> <li>• Electrolyte and metabolic disturbances</li> <li>• Dry mouth, headache</li> <li>• Cramps</li> </ul>	<ul style="list-style-type: none"> <li>• It potentiates digitalis toxicity</li> <li>• Potassium must be supplemented when used alone</li> <li>• It can be combined with a potassium sparing diuretic</li> <li>• Not recommended for children</li> <li>• GI symptoms</li> <li>• Blood dyscrasias</li> <li>• Hypotension, dizziness</li> </ul>
Torsemide	Oral: 10-40 mg as a single or divided dose I.V 10-20 mg	Same as above		

*Note:* It potentiates digitalis toxicity due to hypokalaemia, hence either K<sup>+</sup> is supplemented during its use or a combination of potassium sparing diuretics may be employed



**Table 3.15:** Potassium-sparing diuretics

Drug	Dose	Contraindications/caution	Side effects	Comment
Spironolactone	Oral: 25-100 mg three times a day	<ul style="list-style-type: none"> <li>Hyperkalaemia</li> <li>Anuria</li> <li>Renal failure</li> </ul>	<ul style="list-style-type: none"> <li>GI distress</li> <li>Mental confusion</li> <li>Ataxia</li> <li>Rashes</li> <li>Gynaecomastia</li> <li>Impotence</li> <li>Menstrual abnormalities</li> <li>Hyperkalaemia</li> </ul>	<ul style="list-style-type: none"> <li>Monitor for electrolyte imbalance</li> <li>Most effective when used with thiazide or loop diuretics</li> <li>Risk of hypokalaemia is reduced by combining it with potassium-losing diuretics</li> </ul>
Triamterene	Oral: 100 mg once or twice a day	Same as above	<ul style="list-style-type: none"> <li>Nausea, vomiting, diarrhoea, headache, granulocytopenia, eosinophilia, acidosis, skin rash, orthostatic hypotension, hyperkalaemia</li> </ul>	Same as above
Amiloride	5 mg once a day (max dose 20 mg)	Same as above	<ul style="list-style-type: none"> <li>GI upset, rash, blood dyscrasias, orthostatic hypotension, reduced alertness, acidosis, calcium depletion, hyperkalaemia, minor psychiatric disturbance (rare)</li> </ul>	Same as above

Triamterene and amiloride exert renal effects similar to that of spironolactone (i.e. block  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{H}^+$  exchange in distal tubules) with a major difference that their action does not depend on the presence of aldosterone, hence, are useful in adrenalectomised state. The dose indications and contraindication and side effects are given in the Table 3.15.

#### Carbonic-anhydrase inhibitor (acetazolamide)

It inhibits renal carbonic anhydrase resulting in increased cation excretion, mainly as sodium and potassium together with bicarbonate. The urine becomes alkaline and the diuresis becomes self-limiting as metabolic acidosis develops.

Inhibition of carbonic anhydrase in the eye results in reduction of intraocular pressure by reducing the formation of aqueous humour.

#### Uses

- Adjunctive treatment of CHF
- Certain epilepsies e.g. petit mal
- Chronic simple glaucoma and post-operatively in acute closed angle glaucoma

#### Contraindications

Sodium and potassium depletion, marked renal, hepatic and adenocortical insufficiency, hyperchloraemic acidosis.

#### Side effects

Nausea, vomiting, anorexia, confusion, headache, ataxia, paraesthesias, polyuria, rash, blood dyscrasias

Dose: 250-1 g daily orally

#### Choice of a diuretic

1. Orally administered thiazides and metolazone are the agents of choice in the treatment of mild to moderate cardiac oedema not associated with hyperglycaemia, hyperuricaemia or hypokalaemia.
2. In patients with heart failure or cirrhosis of liver where oedema is associated with secondary hyperaldosteronism, a combination of thiazide or loop diuretic with spironolactone is quite effective.
3. Loop diuretics either alone or in combination of spironolactone or triamterene are the agents of choice in patients with severe heart failure refractory to other diuretics.

4. In severe heart failure, the combination of a thiazide, a loop diuretic and a potassium-sparing diuretic is required.

#### *Indications for high dose parenteral furosemide*

- Acute renal failure
- Forced diuresis for poisoning and hypercalcaemia
- Acute pulmonary oedema
- Decongestive therapy in acute cerebral oedema
- Hypertensive encephalopathy or related emergencies

### SYMPATHOMIMETICS

Sympathomimetic amines activate the adrenergic receptors either directly or release noradrenaline from the sympathetic nerve endings (indirect action). Many drugs have both direct and indirect effects.

1. **Epinephrine (adrenaline) or norepinephrine (noradrenaline):** They stimulate the adrenergic receptors directly. Noradrenaline is employed to support the circulation and elevate the BP in hypotensive states. Vasoconstriction is the major effect, although cardiac stimulation occurs as well. It is used in hypotension and shock.

Adrenaline (epinephrine) is also a pressure agent, has special usefulness in treatment of allergic conditions, especially those associated with anaphylaxis. Adrenaline antagonises the effects of histamine and other mediators on vascular and visceral smooth muscle and is useful in the treatment of bronchospasm or bronchial asthma in children.

2. **Dopamine:** It is an adrenergic agonist. Its effect is dose-dependant.

At low dose, it exerts a positive inotropic effect by direct action of  $\beta_1$ -cardiac receptors and by indirect release of norepinephrine from sympathetic nerve endings in the heart. At lower doses, it acts as vasodilator of renal and mesenteric vessels and facilitates sodium excretion and diuresis. Because of this action, it is used in oliguric conditions associated with intense vasoconstriction as an adjunct to diuretic therapy.

At higher infusion rates interaction with  $\alpha$ -adrenergic receptors result in vasoconstriction, an increase in peripheral vascular resistance and an elevation of

BP. Because of this action, it is used in hypotension and shock.

3. **Dobutamine:** A congener of dopamine with relative selectivity for  $\beta_1$  receptors and with a greater effect on myocardial contractility than on heart rate, is used in treatment of shock and in congestive heart failure in combination with vasodilators. Dobutamine is also used in pharmacological stress testing in conjunction with radionuclide imaging or with echocardiography for the diagnosis of demand-induced myocardial ischaemia.

#### *Beta-receptors Agonists*

Isoproterenol, a direct acting beta-receptors agonist, stimulates the heart, decreases peripheral resistance and relaxes bronchial smooth muscle. It raises the cardiac output and accelerates AV conduction while increasing the automaticity of ventricular pacemakers. It is used in the treatment of AV block and bronchospasm. Selective  $\beta_2$ -receptors agonists (terbutaline, salbutamol, salmeterol, metaproterenol etc.) are used as bronchodilators by inhalation (read bronchodilators)

#### *Alpha-adrenergic Agonists*

Phenylephrine and methoxamine are direct-acting alpha-agonists (stimulants) that raise the BP by causing peripheral vasoconstriction. They are used in treatment of hypotension and paroxysmal supraventricular tachycardia (PSVT). In the latter case, they decrease the heart rate by increasing cardiac vagal tone through reflex baroreceptor stimulation. Phenylephrine is also used as nasal decongestant for the treatment of allergic rhinitis and upper respiratory infections (URI).

#### *Miscellaneous sympathomimetics with mixed actions*

Ephedrine has both direct beta-receptor agonist effect as well as indirect effect by release of norepinephrine on sympathetic nerve endings. It is primarily used as a bronchodilator.

Pseudoephedrine a congener of ephedrine is a less potent bronchodilator, hence, is used as a nasal decongestant.

Metaraminol (mephentine) has both direct and indirect effects on sympathetic nervous system. It was used in the treatment of hypotensive states but is obsolete now-a-days.

**Table 3.16:** Some commonly used sympathomimetics

Drug	Uses	Dose and Route	Side-effects	Comment
Epinephrine (Adrenaline)	<ul style="list-style-type: none"> <li>Anaphylaxis</li> <li>Acute asthma in children</li> <li>Cardiac arrest (asystole)</li> </ul>	300-500 mg SC or IM  (0.3-0.5 ml of 1:1000 dilution, infuse 25-50 mg IV slowly every 5-15 minutes, titrate as needed)	<ul style="list-style-type: none"> <li>Palpitation, tachycardia and sweating</li> <li>Hypotension</li> </ul>	<ul style="list-style-type: none"> <li>Nonselective alpha and beta stimulant, increases BP and HR</li> <li>Bronchodilation</li> </ul>
Norepinephrine (noradrenaline)	<ul style="list-style-type: none"> <li>Shock</li> <li>Hypotension</li> </ul>	2-4 mg base/min IV; titrate according to response	—do—	<ul style="list-style-type: none"> <li>Alpha and <math>\beta_1</math>-stimulant</li> <li>Vasoconstriction predominates</li> <li>Extravasation causes tissue necrosis; infuse through IV cannula</li> </ul>
Isoproterenol	<ul style="list-style-type: none"> <li>Cardiogenic shock</li> <li>Bradyarrhythmias</li> </ul>	0.5-5 mg/min; titrate according to response	—do—	<ul style="list-style-type: none"> <li>Nonselective beta-agonist</li> <li>Increases HR and contractility</li> </ul>
	<ul style="list-style-type: none"> <li>AV block</li> <li>Asthma</li> </ul>	Inhalation		<ul style="list-style-type: none"> <li>Dilates bronchi and tachycardia can also occur</li> </ul>
Dobutamine	<ul style="list-style-type: none"> <li>Refractory CHF</li> <li>Cardiogenic shock</li> <li>Acute oliguric state</li> <li>It is not a dopaminergic</li> </ul>	2.5-25 $\mu\text{g/kg/min}$ IV infusion	—do—	<ul style="list-style-type: none"> <li>Selective <math>\beta_1</math>-agonist with maximum effect on cardiac contractility than HR</li> </ul>
Phenylephrine	Hypotension	2-5 mg SC or IM 0.1-0.5 mg IV	—do—	Selective $\alpha_1$ agonist; useful in hypotension due to spinal anaesthesia
	PSVT	150-800 mg slow IV push		Pressure effect induces vagotonic response
Dopamine	<ul style="list-style-type: none"> <li>Shock</li> <li>Oliguric state</li> </ul>	<ul style="list-style-type: none"> <li>2-5 <math>\mu\text{g/kg/min}</math> IV (dopaminergic range, vasodilator effect)</li> <li>5-10 <math>\mu\text{g/kg/min}</math> IV (dopaminergic and beta range)</li> <li>10-20 <math>\mu\text{g/kg/min}</math> IV (beta range)</li> <li>20-50 <math>\mu\text{g/kg/min}</math> IV (alpha range)</li> </ul>	—do—	Pharmacological effects are dose-dependent; renal and mesenteric vasodilation predominates at lower doses; cardiac stimulation and vasoconstriction develop as the dose is increased
Bromocriptine	<ul style="list-style-type: none"> <li>Prolactinoma</li> <li>Amenorrhoea-galactorrhoea syndrome</li> <li>Acromegaly</li> <li>Parkinsonism</li> </ul>	2.5 mg orally bid or tid  5-15 mg orally tid or qid 1.25 to 2.5 mg at bedtime, increased upto 10-40 mg/day in divided doses	Nausea, vomiting, dizziness, fatigue postural hypotension, vaso-spasm, CNS	<ul style="list-style-type: none"> <li>It is dopaminergic agonist</li> <li>Selective agonist of <math>D_2</math> receptor; inhibits prolactin secretion</li> <li>Useful for parkinsonism sensitive to levodopa</li> <li>Lowers growth hormone levels in majority of patients with acromegaly</li> </ul>

**Dopaminergic Agonists** The dopamine ( $D_2$ ) receptors agonist bromocriptine is used to suppress prolactin secretion in prolactinoma and galactorrhoea-amenorrhoea syndrome.

Apomorphine, another  $D_2$  receptor agonist is used to induce vomiting.

#### *Dose, Route and Indications*

They are tabulated (Table 3.16)

## PARASYMPATHOMIMETICS

These include;

### Cholinergic Agonists

They stimulate cholinergic receptors. Bethanechol is the only cholinergic agonist in general use, stimulates gastrointestinal and genitourinary smooth muscle with minimal effect on CVS

### Uses

1. Treatment of urinary retention without outflow tract obstruction
2. Postvagotomy gastric atony
3. Gastroesophageal reflux disease

Pilocarpine and carbachol are topical cholinergic agonists used in the treatment of glaucoma.

### Cholinesterase Inhibitors

Cholinesterase inhibitors diminish the inactivation of acetylcholine, hence, enhance parasympathetic stimulation. Organophosphorous compound are potent cholinesterase inhibitor, used principally as insecticides and are primarily of toxicological interest.

The drugs used clinically include;

1. *Physostigmine*—a tertiary amine penetrates the CNS well, hence, acts as central cholinesterase inhibitor. Dose is 1-2 mg IV slowly, when as required.
2. *Neostigmine*, *pyridostigmine*, *edrophonium* etc are quaternary amines, do not penetrate CNS, act at neuromuscular junction.

### Uses

- i. For treatment of myasthenia gravis
- ii. For termination of neuromuscular blockade following general anaesthesia
- iii. Reversal of intoxication by agents with a central anticholinergic action
- iv. Cholinesterase inhibitors induce vagotonic response in the heart and may be useful in terminating attacks of paroxysmal supraventricular tachycardia. Edrophonium 5 mg IV (after 1 mg as test dose) is used for this purpose

## DRUG USED IN CNS AND PSYCHIATRY

### ANALGESICS AND ANTIPYRETICS

Analgesics are the drugs that relieve pain while antipyretics bring the temperature down during pyrexia.

Assessment of pain is essential for its correct management because pain is subjective phenomenon based on the individual own interpretation and clinical signs. Pain may be acute or chronic having variable characteristics. The pain may be organic or psychogenic in origin. An attempt should always be made to find out the cause of pain and to treat it appropriately; for example, use of hormone or hormone antagonists in gynaecological pain; and consider alternative approaches or adjunct therapy if pain is not controlled.

#### Analgesic Ladder

The WHO analgesic ladder (Fig. 3.1) ascending from non-opiates through weak opiates to strong opiates according to severity of pain (1. mild 2. moderate 3. severe) is widely regarded as best approach to the management of acute pain, chronic non-malignant pain and chronic malignant pain. The goal of treatment in all types of pain irrespective of its cause is to achieve symptom relief and improve the patient's quality of life.

#### A. Non-opiate Analgesics

#### 1. Salicylates (aspirin, salicylamide, sodium salicylate)

#### Actions

All exert analgesic, antipyretic and anti-inflammatory actions which are due to an inhibition of prostaglandin synthesis (cyclo-oxygenase inhibitor). Their analgesic

3	Strong opiate analgesic e.g. morphine, oxycodone
2	Weak opiate analgesics e.g. dextropropoxyphene, codeine, tramadol etc.
1	Non-opiate analgesic e.g. aspirin, paracetamol, NSAIDs etc.

**Fig 3.1:** WHO analgesic ladder

effect is due to their peripheral anti-inflammatory action as well as a central effect on hypothalamus. Aspirin in lower doses also inhibit platelet aggregation (anti-platelet action).

#### Uses

1. They are used as anti-inflammatory agents in the treatment of rheumatoid arthritis, rheumatic fever, osteoarthritis and other rheumatic conditions.
2. Aspirin is used in acute painful conditions such as headache, arthralgia, myalgia and other non-specific conditions requiring mild analgesia.
3. It is also used as an antipyretic.
4. Aspirin in lower doses (100-300 mg) is used as an antiplatelet agent (Read anti-platelet agents) in the treatment of certain vascular disorders e.g. transient ischaemic attacks, angina. Prophylactically, it is used as an antiplatelet in CVA, post-myocardial angina, atherogenesis in diabetes and hypertension.

#### Contraindications

- Peptic ulcer and erosive gastritis
- Lactation
- Bleeding disorders
- Previous hypersensitivity
- Concomitant use of probenecid or other uricosuric agents (reduces uricosuric effect)

#### Caution

- Bronchial asthma
- Low prothrombin time
- Full term pregnancy

#### Side effects

- Gastric irritation, pain abdomen and gastric erosion, haematemesis.
- Asthma
- Previous allergy
- Reye's syndrome. The drug controller has recommended that aspirin should not be given to children below 12 years of age because of increased risk of development of Reye's syndrome.

**Dose** 600 mg orally to be repeated after 4 hours.

### p-Aminophenol Derivatives (Paracetamol)

#### Actions

These compounds exert analgesic and antipyretic activity but no anti-inflammatory effect. Their mechanism of action is similar to aspirin.

#### Uses

Relief of pain, fever (pyrexia)

**Contraindication:** Analgesic nephropathy

**Dose:** 1-2 g orally 3-4 times a day (max 8 g/day)

**Side effects:** Nausea, vomiting, dyspepsia, haematological changes; large dose produce hepatotoxicity and analgesic nephropathy.

### Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

Besides aspirin, there are several additional nonsteroidal anti-inflammatory drugs (NSAIDs) to treat musculoskeletal and inflammatory disorders.

#### Actions

All these drugs are cyclo-oxygenase inhibitor (Cox-inhibitor), hence, interfere with prostaglandin synthesis. They have analgesic, anti-inflammatory and antipyretic properties.

Research has further revealed two isoforms of cyclo-oxygenase (Cox). The first isoform (Cox-I) is present in cells and tissues including, stomach, kidneys while Cox-2 is induced in response to inflammation, hence, Cox-I inhibitor are responsible for most of the side effects such as gastric erosion, renal toxicity while Cox-2 inhibitors (Box 3.4) are presumed to be safe, more potent with fewer side-effects devoid of gastric and renal toxicity. Most of the NSAIDs have property to inhibit both Cox I and 2.

#### Uses

1. They are used as anti-inflammatory analgesic drugs in variety of pain due to musculoskeletal disorders (low back pain, soft tissue rheumatism). Their analgesic property is comparable to paracetamol.



**Box 3.4: Cox-2 inhibitors**

<i>A. Partially selective cyclo-oxygenase-2 inhibitors</i>	
Aceclofenac	100-200 mg/day
Meloxicam	7.5-15 mg/day
Nabumetone	500-1500 mg/day
<i>B. Selective Cox-2 inhibitors</i>	
Rofecoxib	12.5-25 mg/day
Celecoxib	

2. They are used as anti-inflammatory drugs for treatment of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and inflammatory bowel disease.

*Safety profile*

Recent evidence on 7 drugs have put some commonly used NSAIDs into three categories (Box 3.5).

**Box 3.5: Safety profile of NSAIDs**

1. <b>Low risk</b>	Dose	Side effects
Ibuprofen	< 1600 mg/day	Dyspepsia, GI bleeding, rarely thrombocytopenia
<b>2. Average risk</b>		
• Diclofenac	75-150 mg/day	• Epigastric pain, nausea, headache, dizziness, rash, oedema, peptic ulcer, GI bleed, hepatic and renal toxicity
• Indomethacin	75-150 mg/day	• GI intolerance, dizziness, CNS effects, blood dyscrasias
• Naproxen	500-1000 mg/day	• Rash, GI intolerance, tinnitus, vertigo, blood dyscrasias
• Piroxicam	10-30 mg/day	• GI disturbance, oedema, CNS effects, malaise, tinnitus
<b>3. High risk</b>		
Azapropazone	1200-1800 mg/day	

*Side Effects*

- GI tract; nausea, vomiting, abdominal pain and haematemesis due to acute gastric erosion
- Fluid retention
- Nephrotoxicity—interstitial nephritis
- Skin—rash
- Hepatotoxicity

- Rarely asthma and anaphylaxis

**Opiates Analgesic**

Weak opiates such as dextropropoxyphene, codeine, dihydrocodeine are used along with aspirin and paracetamol for relief of moderate pain.

The side effects of codeine are nausea and constipation. Strong opiates (morphine, oxycodone, fentanyl, hydromorphone, methadone and pentazocine) are strong analgesic but habit-forming and constipating agents.

*Indications*

- As an antitussive agent e.g. dihydrocodeine
- As an anti-diarrhoeal agent e.g. codeine
- Severe continuous pain such as pain of acute myocardial infarction, cancer pain etc.
- Acute musculoskeletal pain not responding to non-opiate analgesic. They may be added as adjunctive therapy..
- Anaesthetic premedication

*Doses and Side Effects*

Table 3.17.

*Contraindications of narcotic analgesics*

- Bronchial asthma
- Severe liver disease
- Head injury or raised intracranial tension
- Respiratory depression

**Anticonvulsant and Antiarrhythmics as Analgesics**

Anticonvulsants and antiarrhythmics increase the threshold for pain, hence, are useful in neuropathic pain such as trigeminal neuralgia, diabetic neuropathy, post-herpetic neuralgia.

These include:

Phenytoin	300 mg/day
Carbamazepine	200-300 mg 6 hrly
Clonazepam	1 mg 6 hourly
Mexiletine	150-300 mg at 6-12 hours intervals
Sodium valproate	400-600 mg/day
Gabapentine	

**Table 3.17:** Narcotic analgesic; usual dosage and intervals

Drug	Parenteral dose (mg)	Oral dose (mg)	Side effects	Comment
Codeine	30-60 q 4 hr	30-60 q 4 hr	Nausea, constipation dependence, CNS depression, hypotension, respiratory depression, decreased urine output	• It is also used as an anti-tussive agent
Morphine	10 q 4 hr	60 q 4 hr	Constipation, respiratory depression, addiction, diaphoresis, nausea, vagotonic bradycardia	• To be used for short time
Hydromorphone	1-2 q 4 hr	2-4 q 4 hr	Same	• Short acting than morphine
Pethidine	50-100 to be repeated	—	Similar to morphine	—
Methadone	10 q 6-8 hr	20 q 6-8 hr	Similar	• Delayed sedation due to long action
Pentazocin	30-60 mg 4 hrly	15-30 mg 6-8 hrly	• Sedation, dizziness, hallucinations, nausea vomiting, diaphoresis, tachycardia, HT and respiratory depression	
Fentanyl	—	—	—	Transdermal patch used as alternative to morphine
Antidote to opiates is naloxone				

**Tricyclic antidepressants as analgesics**

These agents are extremely useful for the management of patients with chronic pain though they have been developed for the treatment of depression. The mechanism of action is unknown. The analgesic effect of antidepressants has a (i) rapid onset of action and occurs at a lower dose that is required for treatment of depression (ii) patient who are not depressed also get relief of chronic pain with these drugs (iii) there is evidence that they potentiate the analgesic effects of opiates, hence, are useful adjuncts for treatment of intractable or severe pain of malignant tumours. The painful conditions that respond to antidepressants are given in Box 3.6.

**Doses**

- Amitriptyline 25-300 mg orally in divided doses in a day
- Imipramine 75-400 mg/day in divided doses
- Doxepin 75-400 mg/day in divided doses

**Box 3.6:** Painful conditions that respond to tricyclic antidepressants

- Postherpetic neuralgia
- Diabetic neuropathy
- Tension headache
- Migrain headache
- Rheumatoid arthritis
- Chronic low back pain
- Cancer

**Antiepileptics or Anticonvulsants**

A seizure is defined as a paroxysmal event due to abnormal excessive hypersynchronous discharges from an aggregate of CNS neurons.

Epilepsy is different from seizure. It is defined as a condition in which a person has recurrent seizures due to a chronic underlying process. This definition implies that a person with a single seizure or recurrent seizures due to correct or removable circumstances does not necessarily have epilepsy. Epilepsy refers to a clinical

phenomenon rather than a single disease. The classification of seizures is given in Box 3.7.

**Box 3.7: Classification of seizures**

**1. Partial seizures**

- A. Simple partial seizures (with motor, sensory, autonomic or psychic signs). Consciousness is preserved.
- B. Complex partial seizure where consciousness is lost.
- C. Partial seizures with secondary generalisation (tonic-clonic variety).

**2. Primary Generalised Seizure**

- A. Absence (Petit mal). Common in children
- B. Tonic-clonic (grand mal)
- C. Tonic
- D. Myoclonic

**3. Unclassified**

- A. Neonatal seizure
- B. Infantile spasms (seen in < 14 of age)

**Jacksonian Epilepsy (Focal Epilepsy)**

It implies partial motor seizures with beginning of abnormal motor movements in a restricted region such as fingers or toes and gradually progressing over seconds to minutes to include a large portion of the extremity or whole extremity.

**Todd's Paralysis**

The patients of Jacksonian fits experience a localised paralysis or paresis due to exhaustion of hyperexcitable neurons that occurs minutes to many hours in the involved region following the seizure. Recovery is the rule in this phenomenon.

**Epilepsia Partialis Continua**

It implies focal or partial seizure that may continue for hours or days. This condition is often refractory to medical therapy.

**Complex-Partial Seizures**

These are characterised by focal seizural activity accompanied by inability to respond to visual and verbal commands during seizure. The patient is unconscious during seizures. It has three stages.

- i. Aura (pre-ictal phase)

- ii. Ictal phase

- iii. Post ictal phase - e.g. confusion, automatism or behavioural changes.

**Absence Seizures (Petit mal)**

These are common in children, characterised by sudden, brief lapses of consciousness accompanied by subtle bilateral motor signs such as rapid blinking of eyelids, chewing movements or clonic movements of the hands. The EEG is characteristic with spike-and-wave discharge.

**Grand Mal (Tonic-Clonic) Seizures**

These are generalised seizures which begin abruptly without warning and have tonic phase (tonic contraction of the muscles throughout the body) and clonic phase (periods of muscle relaxation or tonic muscle contraction leading to muscular flaccidity, excessive salivation and bowel and bladder incontinence). The conscious is lost during seizure and it may be prolonged.

**Tonic Seizures**

These are variants of grand mal that include pure tonic contractions of the muscles lasting only for a few seconds.

**Atonic Seizures**

They are characterised by sudden loss of muscle tone lasting for 1 to 2 seconds with impaired consciousness. There is no postictal confusion. A very brief seizure may cause a quick head drop or nodding movement while a longer will cause the patient to collapse and sudden fall.

**Myoclonic Seizures**

These are characterised by myoclonic jerks i.e. a sudden and brief muscle contractions that may involve one part of the body or the entire body. These are generalised seizures, hence, consciousness is lost. The EEG is characteristic i.e. bilateral synchronous spike-and-wave discharges.

**Neonatal Seizures**

These are characterised by brief episodes of apnoea, eye deviation, eye blinking or repetitive movements of arm

and legs, hence, are subtle in manifestations. An EEG is critical for diagnosis in such cases.

### Infantile Spasms

These are seen in infants (< 1 yr of age) and are characterised by abrupt movements of head, trunk or limbs that often occur in clusters (groups) of 10-20 movements per episode.

The classic spasm is sudden flexion of the neck and abdomen with extension of the limbs (Jack-Knife seizures)

The EEG shows hypoarrhythmia which consists of high-voltage slow multifocal spikes and a variety of other pleomorphic abnormalities.

### Febrile Seizures/Convulsions

These are the most common seizures seen in childhood, are associated with fever but without evidence of CNS infection or other defined causes. The patients often have a family history of either febrile convulsions or epilepsy. The typical scenario is a child who develops tonic-clonic seizure during a rising phase of temperature of a febrile episode (i.e. during the first day). These seizures may be

simple partial (no loss of consciousness) or complex partial (loss of consciousness). They may be recurrent in one third cases.

#### Causes

See the Table 3.18.

#### Uses

These drugs are used for

1. Control of various types of seizures/epilepsy
2. Phenytoin is used for digitalis-induced arrhythmias
3. Phenytoin, carbamazepine and valproate, gabapentine are used for control of pain due to trigeminal neuralgia, diabetic neuropathy and other neuropathies
4. Carbamazepine is used for prophylaxis of manic-depressive illness.

#### Choice of Drug in Epilepsy

Table 3.19.

Drugs, Dosage and side effects (Table 3.20)

**Table 3.18:** The causes of seizures

Neonates (< 1 month)	Infants and children (< 12 yrs)	Adolescent	Adults	Old persons
<ul style="list-style-type: none"> <li>• Perinatal hypoxia and ischaemia</li> <li>• Intracranial bleed or trauma</li> <li>• Meningitis</li> <li>• Metabolic abnormalities (hypoglycaemia, hypocalcaemia, hypomagnesemia, pyridoxine deficiency)</li> <li>• Drug withdrawal (babies born to mothers using neurotoxic drugs)</li> <li>• Developmental disorders</li> <li>• Genetic disorders (metabolic and degenerative)</li> </ul>	<ul style="list-style-type: none"> <li>• Febrile seizures</li> <li>• Genetic disorder (metabolic or degenerative)</li> <li>• Meningitis, encephalitis</li> <li>• Developmental disorders</li> <li>• Head trauma</li> <li>• Idiopathic</li> </ul>	<ul style="list-style-type: none"> <li>• Head trauma</li> <li>• Genetic disorders</li> <li>• Brain tumor</li> <li>• Illicit drug abuse</li> <li>• Idiopathic</li> <li>• Meningitis, encephalitis</li> </ul>	<ul style="list-style-type: none"> <li>• Head trauma</li> <li>• Alcohol withdrawal</li> <li>• Illicit drug abuse</li> <li>• Brain tumour</li> <li>• Idiopathic</li> </ul>	<ul style="list-style-type: none"> <li>• CVA</li> <li>• Brain tumor</li> <li>• Alcohol withdrawal</li> <li>• Metabolic diseases (uraemia, hepatic failure, electrolyte disturbances, hypoglycaemia)</li> <li>• Alzheimer's disease and other degenerative disorder</li> <li>• Idiopathic</li> </ul>

**Table 3.19:** Choice of antiepileptic drugs in various types of epilepsy

Epilepsy	First line drug (s)	Alternatives
1. Grand mal (tonic-clonic)	<ul style="list-style-type: none"> <li>Phenytoin</li> <li>Carbamazepine</li> <li>Sodium valproate</li> <li>Primidone</li> </ul>	<ul style="list-style-type: none"> <li>Phenobarbitone</li> <li>Clobazam</li> <li>Clonazepam</li> </ul>
2. Focal (partial) seizures	-do-	<ul style="list-style-type: none"> <li>Phenobarbitone, primidone, lamotrigene, Gabapentine</li> </ul>
3. Petit mal	<ul style="list-style-type: none"> <li>Sodium valproate</li> </ul>	<ul style="list-style-type: none"> <li>Ethosuximide</li> </ul>
4. Myoclonic	<ul style="list-style-type: none"> <li>Sodium valproate</li> <li>Clonazepam</li> </ul>	<ul style="list-style-type: none"> <li>Carbamazepine</li> <li>Phenytoin</li> </ul>
5. Status Epilepticus	<ul style="list-style-type: none"> <li>Clonazepam</li> <li>Phenytoin</li> </ul>	<ul style="list-style-type: none"> <li>Diazepam, Lorazepam</li> <li>Paraldehyde</li> </ul>

### Pregnancy, Lactation and Antiepileptic Drugs

- Most women with epilepsy who become pregnant will have an uncomplicated gestation and deliver a normal baby. During pregnancy, there may be a change in frequency and severity of seizures, hence, monitor the serum level of anti-epileptic drugs and see the patient at frequent intervals.
- There is an increased risk of teratogenicity associated with use of antiepileptic drugs; for example neural tube defects associated with carbamazepine, phenytoin and valproate. Therefore, woman who become pregnant while taking these drugs should be advised antenatal screening ( $\alpha$ -fetoprotein measurement and USG scan during second trimester).
- To counteract the neural tubal defect, folic acid 5 mg daily should be recommended before and during pregnancy.
- To reduce the risk of neonatal bleeding associated with the use of carbamazepine, phenytoin and phenobarbitone, prophylactic vit K, is recommended for mothers before delivery and as well as for neonates.
- Breast feeding is acceptable with all antiepileptic drugs taken in normal doses except barbiturates and ethosuximide.
- Current recommendations are that women who become pregnant on antiepileptic drug should continue it during pregnancy in effective or optimal dose. They are advised to continue folate throughout pregnancy.

- Drugs used in pregnancy include phenytoin, carbamazepine and valproate (Table 3.21).

### PSYCHOTROPIC DRUGS

*Definition:* Drugs used to treat psychiatric illnesses are collectively called as *psychotropic drugs*. They are classified according to their mode of action (Table 3.22).

### ANTI-PSYCHOTIC (NEUROLEPTIC) DRUGS

*Actions:* These drugs act by blocking central dopamine receptors ( $D_1$  and  $D_2$ ), thus reduce the psychomotor excitement and control many of the symptoms of psychotic disorder without causing disinhibition, confusion or sleep. They possess sedative, hypnotic and antipsychotic properties.

#### Uses

- Acute schizophrenia
- To prevent relapse in chronic schizophrenia
- Mania
- Acute confusional states
- In low doses, they are used to treat anxiety.
- Phenothiazines are useful in the treatment of vomiting (antiemetic), alcoholism, intractable hic-cups, over-dosage of hallucinogenic compounds and choreiform movements. Promethazine is used as an anti-allergic agent.

#### Contraindications

- Subcortical brain damage
- Coma



Table 3.20: Commonly used antiepileptic drugs

Drug	Action	Uses	Dose and Intervals	Neurologic	Side effects	Drug interactions
Phenytoin or dilantin	It increases the seizure threshold in the motor cortex possibly by interfering with movements of ions e.g. $\text{Na}^+$ and $\text{Ca}^{++}$ through cell membranes	<ul style="list-style-type: none"> <li>• Grand mal seizure</li> <li>• Psychomotor seizures</li> <li>• Focal onset seizure</li> <li>• Cardiac arrhythmias especially digitalis-induced</li> <li>• Trigeminal neuralgia</li> <li>• Seizures following head injury or neurosurgery</li> <li>• Pain due to diabetic or other neuropathy</li> </ul>	<p><b>Oral:</b> Adults: Initially 3-4 mg/kg daily or 200-300 mg daily (as a single dose or two divided doses). Usual dose 200-400 (max 600 mg/day)</p> <p>Children: Usual dose 4-6 mg/kg (Max. 300 mg)</p> <p><b>Injections</b></p> <p>1. <i>Status Epilepticus</i></p> <ul style="list-style-type: none"> <li>• Adults: Initially 10-15 mg/kg IV slowly (not exceeding 50 mg/min) then 100 mg IV or orally every 6-8 hours</li> <li>• Children: 10-20 mg (kg IV slowly</li> </ul> <p>2. <i>Neurosurgery prophylaxis</i></p> <ul style="list-style-type: none"> <li>• 250 mg IV slowly 6-12 hourly</li> </ul> <p>3. <i>Cardiac arrhythmias</i></p> <ul style="list-style-type: none"> <li>• 3-5 mg/kg by slow IV infusion; repeat if necessary</li> </ul>	<ul style="list-style-type: none"> <li>• Ataxia</li> <li>• Confusion</li> <li>• Incoordination</li> <li>• Cerebellar features e.g. ataxia</li> </ul>	<p><b>Systemic</b></p> <ul style="list-style-type: none"> <li>• Gum hyperplasia</li> <li>• Lymph node enlargement/hyperplasia</li> <li>• Osteomalacia</li> <li>• Excessive hair growth</li> <li>• Coarsening of facial features</li> <li>• Skin rash</li> </ul>	<ul style="list-style-type: none"> <li>• Isoniazid and sulphonamides increase its levels</li> <li>• Phenobarbitone and carbamazepine decrease its levels</li> </ul>
Carbamazepine	It increases seizure threshold by inhibiting $\text{Na}^+$ -dependent action potentials	<ul style="list-style-type: none"> <li>• Tonic-clonic seizure</li> <li>• Focal onset seizure</li> <li>• Trigeminal neuralgia</li> <li>• Prophylaxis in manic-depressive illness (mood stabiliser/elevator)</li> </ul>	<p><b>Oral</b></p> <ul style="list-style-type: none"> <li>• Adults, start 100-200 mg once or twice daily and then increase slowly to 400 mg 2-3 times/day.</li> <li>• Children <ul style="list-style-type: none"> <li>• upto 1 yr: 100-200 mg/d</li> <li>• 1-5 yrs: 200-400 mg/d</li> <li>• 6-10 yrs: 400-600 mg/d</li> <li>• 11-15 yrs: 600-1000 mg/d</li> <li>• Total daily dose is given in divided doses</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Ataxia</li> <li>• Diplopia</li> <li>• Vertigo</li> <li>• Dizziness</li> </ul>	<ul style="list-style-type: none"> <li>• Aplastic anaemia</li> <li>• Leukopenia</li> <li>• GI upset</li> <li>• Hepatotoxicity</li> </ul>	<ul style="list-style-type: none"> <li>• Level decreased by phenobarbitone and phenytoin</li> <li>• Level increased by erythromycin and isoniazid</li> </ul>
Valproic acid (monotherapy or adjuvant therapy)	It increases brain levels of the inhibitory neurotransmitter GABA	<ul style="list-style-type: none"> <li>• Tonic-clonic generalised seizures</li> <li>• Focal seizures</li> <li>• Absence seizures</li> <li>• Myoclonic seizures</li> <li>• Prophylaxis in manic-depressive illness (mood elevator/stabiliser)</li> </ul>	<p><b>Oral</b></p> <p>Adults 600 mg bid then increase by 200 mg at 3 days interval (max 2.5 g/day)</p> <p>Children &lt;20 kg: 200mg initial dose &gt; 20 kg: Initial dose is 400 mg daily and then increase slowly to achieve control (max 35 mg/day)</p>	<ul style="list-style-type: none"> <li>• Ataxia</li> <li>• Tremors</li> <li>• Drowsiness or sedation</li> </ul>	<ul style="list-style-type: none"> <li>• Liver toxicity</li> <li>• Thrombocytopenia</li> <li>• GI upset</li> <li>• Weight gain</li> <li>• Alopecia</li> <li>• Skin rash</li> </ul>	<p>Levels decreased by phenobarbitone, carbamazepine and phenytoin</p>

Contd..

Table contd...

Drug	Action	Uses	Dose and Intervals	Side effects	
				Neurologic	Systemic
Primidone (mysoline)	It is converted in the body to phenobarbitone and its anti-epileptic properties are due to both phenobarbitone and the parent drug	<ul style="list-style-type: none"> <li>• Tonic-clonic seizure</li> <li>• Focal onset seizure</li> </ul>	<p><b>Oral</b></p> <ul style="list-style-type: none"> <li>• Start as 125-250 mg at bed time and double the dose after 3 days, then increase it by 250 mg after every 3 days till control is achieved. Usual dose 750-1000 mg bid or tid.</li> </ul>	Same as phenobarbitone	
Phenobarbitone	It exerts anti-epileptic effect by CNS depression	<ul style="list-style-type: none"> <li>• Tonic-clonic seizure</li> <li>• Focal-onset seizure</li> <li>• As a hypnotic</li> <li>• Used as an anaesthetic agent</li> <li>• Status epilepticus</li> <li>• Pre-eclampsia</li> </ul>	<p><b>IV.</b></p> <p>For status: epilepticus 400-800 mg</p> <p>Edampsia: 300 mg both are given in divided doses 2-4 hourly</p> <p><b>Oral:</b> Adult: Start with 500 mg and increase slowly to 1-1.5 g/ daily</p> <p><b>Children:</b> Start 250 mg and increase upto 1.0 g/ day in divided doses</p>	<ul style="list-style-type: none"> <li>• Sedation</li> <li>• Dizziness</li> <li>• Confused state</li> <li>• Depression</li> <li>• Decreased libido</li> </ul>	<ul style="list-style-type: none"> <li>• Skin rash</li> </ul> <p>Levels increased by valproic acid and phenytoin</p>
Ethosuximide (Zarontin)	It increases the seizure threshold by CNS depression	<ul style="list-style-type: none"> <li>• Petit mal</li> </ul>	<p><b>Oral:</b> Adult: Start with 500 mg and increase slowly to 1-1.5 g/ daily</p> <p><b>Children:</b> Start 250 mg and increase upto 1.0 g/ day in divided doses</p>	<ul style="list-style-type: none"> <li>• Ataxia</li> <li>• Lethargy</li> <li>• Headache</li> </ul>	<ul style="list-style-type: none"> <li>• GI upset</li> <li>• Skin rash</li> <li>• Bone marrow depression</li> </ul>
Gabapentine	Being a structural analogue of GABA, increases GABA synthesis and release	<ul style="list-style-type: none"> <li>• Focal onset seizure</li> <li>• Diabetic neuropathy</li> <li>• Trigeminal neuralgia</li> </ul>	<p><b>Oral:</b> Adult</p> <p>1st day-300 mg once/day</p> <p>2nd day-300 mg twice/day</p> <p>3rd day-300 mg thrice/day</p> <p>Now increase the dose slowly three times a day to reach max of 800 mg tid.</p> <p><b>Children:</b> Not recommended</p> <p>150-500 mg bid.</p>	<ul style="list-style-type: none"> <li>• Sedation</li> <li>• Dizziness</li> <li>• Ataxia</li> <li>• Fatigue</li> </ul>	<ul style="list-style-type: none"> <li>• GI upset</li> </ul>
Lamotrigine	It suppresses burst-firing neurons by inhibiting Na <sup>+</sup> -dependent action potentials	<ul style="list-style-type: none"> <li>• Focal onset seizure</li> </ul>	<p><b>Children:</b> Not recommended</p> <p>150-500 mg bid.</p>	<ul style="list-style-type: none"> <li>• Dizziness</li> <li>• Diplopia</li> <li>• Sedation</li> <li>• Ataxia</li> <li>• Headache</li> </ul>	<ul style="list-style-type: none"> <li>• Skin rash</li> <li>• Stevens-Johnson syndrome</li> </ul>
Clonazepam	CNS depressant	<ul style="list-style-type: none"> <li>• Absence seizure</li> <li>• Myoclonic seizure</li> </ul>	<p><b>Oral</b></p> <p><b>Adult:</b> Start 0.5 mg bid, then increase 0.5 mg after 3-7 days to reach upto 4-8 mg/day.</p> <p><b>Children</b></p> <p>2-5 yrs. Initial 0.5 mg in two divided doses then increase it upto 1.5 to 3 mg/day.</p> <p>6-12 yrs 0.75 mg in two divided doses, then increase to reach 3-6 mg/day</p>	<ul style="list-style-type: none"> <li>• Lethargy</li> <li>• Dizziness</li> <li>• Sedation</li> <li>• Ataxia</li> </ul>	<ul style="list-style-type: none"> <li>• Anorexia</li> </ul>

**Table 3.21:** Safety of common antiepileptics during pregnancy

Drugs	Suspected adverse effects	Comments
Phenytoin	Fetal hydantoin syndrome (Facial dysmorphism, cleft palate and lip, cardiac defects, digital hypoplasia and nail dysplasia)	
Carbamazepine and Sodium valproate	Increased risk of neural tube defects Aminocentesis should be offered if abnormality suggested	<ul style="list-style-type: none"> <li>• <math>\alpha</math>-fetoprotein should be measured at 16 weeks gestation</li> </ul>
Phenobarbitone and primidone	Increased risk of nonspecific defects	<ul style="list-style-type: none"> <li>• Consider possibility of neonatal withdrawal syndrome</li> </ul>
Benzodiazepines	Increased risk of oral clefts syndrome	<ul style="list-style-type: none"> <li>• Neonatal withdrawal</li> <li>• Taper dose and withdraw before delivery if possible.</li> </ul>
Newer drugs e.g. gabapentin, lamotrigine, topiramate, vigabatrin	Risk unknown	<ul style="list-style-type: none"> <li>• Older agents are preferred during pregnancy at present</li> </ul>

**Table 3.22:** Classification of psychotropic drugs

Action	Main Groups	Uses
Antipsychotic	<ul style="list-style-type: none"> <li>• Phenothiazines</li> <li>• Butyrophenones</li> <li>• Thioxanthenes</li> <li>• Substituted Benzamides</li> <li>• Benzisoxazole</li> </ul>	Acute and chronic schizophrenia, acute confusion, mania
Antidepressant	<ul style="list-style-type: none"> <li>• Tricyclic and related drug</li> </ul>	<ul style="list-style-type: none"> <li>• Depressive illness, obsessive compulsive disorder, nocturnal enuresis, neuropathic pain disorders</li> </ul>
Mood-Stabilising	<ul style="list-style-type: none"> <li>• Selective 5 HT (serotonin) inhibitors</li> <li>• Tetracyclic</li> <li>• Mono-oxidase inhibitors</li> <li>Lithium</li> </ul>	<ul style="list-style-type: none"> <li>• Depression where sedation is not required</li> <li>• Obsessive-compulsive disorders.</li> </ul> <p>Depressive illness Depressive illness, phobic disorders Prophylaxis of mania depression, acute mania, mood disorders Prophylaxis of manic depression</p>
Anxiolytics	<p>Carbamazepine Benzodiazepines</p> <p>Beta-blockers Buspirone, Azapirone</p>	<ul style="list-style-type: none"> <li>• Anxiety and anxiety related disorders</li> <li>• Insomnia</li> <li>• Alcohol withdrawal</li> </ul> <p>Anxiety (somatic symptoms) Anxiety disorders</p>

- Circulatory collapse
- Impaired liver function
- Blood dyscrasias

*Side-effects* (Box 3.8)

*Dosage:* The dosage of various groups of antipsychotic drugs is given in the Box 3.9.

**Box 3.8: Adverse effects of antipsychotic drugs****A. Extrapyramidal**

- Acute dystonia
- Parkinsonism
- Tardive dyskinesia
- Akathisia

**B. Autonomic**

- Hypotension
- Failure of ejaculation

**C. Anticholinergic (atropine-like effects)**

- Dry mouth
- Urinary retention
- Constipation
- Blurred vision

**D. Metabolic**

- Weight gain

**E. Rare-effects**

- Hypersensitivity
- Cholestatic jaundice
- Leucopenia
- Skin reactions

**F. Miscellaneous (others)**

- Precipitation of glaucoma
- Galactorrhoea-Amenorrhoea
- Cardiac arrhythmias
- Seizures
- Retinal degeneration (with thioridazine in high doses)

has to be monitored by blood count and it must be stopped if neutropenia develops.

*Indications of phenothiazines* (Parenteral or oral). The parenteral therapy is given during acute conditions.

1. As an antipsychotic drug: They are used in the treatment of acute schizophrenia and to prevent its relapse.
2. Mania and acute confusional states.
3. As an anxiolytic and hypnotics.
4. Antiemetic. Used to prevent nausea and vomiting. They block dopamine receptors in chemoreceptor trigger zone.
5. Alcoholism
6. Premedication in anaesthesia
7. Intractable hic-cups
8. Overdosages of hallucinogenic compounds, e.g. LSD
9. Promethazine is used as an anti-allergic
10. To prevent choreiform movements in rheumatic chorea
11. Induction of hypothermia

*Toxicity (Overdosage) of Phenothiazines*

Phenothiazines cause less depression of consciousness and respiration than other sedatives. The features of toxicity include;

*I. CVS:* Hypotension, shock, sinus tachycardia and cardiac arrhythmias (particularly with thioridazine)

*Treatment:* Arrhythmias may respond to correction of hypoxia and acidosis but antiarrhythmic drugs may also be needed.

*II. Dystonic reactions* (particularly with prochlorperazine and trifluoperazine) and convulsions may occur in severe cases

*Treatment:* Dystonic reactions are rapidly abolished by injection of drugs such as benztropine or procyclidine.

**Antidepressants and Mood Disorders**

*Depression:* It is a disorder of mood, behaviour and affect. It is unipolar primary affective disorder in which patient is gloomy, despondent and sad (depressed mood).

**Box 3.9: Antipsychotic drugs dosage**

Group	Drug	Usual dose
Phenothiazines	• Chlorpromazine	100-150 mg/day
	• Thioridazine	50-80 mg/day
	• Trifluoperazine	5-30 mg/day
	• Fluphenazine	20-100 mg/day
Butyrophenones	Haloperidol	5-30 mg/day
Thioxanthenes	Flupenthixol	40-200 mg fortnightly
Diphenylbutyl piperidines	Plmozide	4-30 mg/day
Substituted benzamides	• Sulpiride	600-1800 mg/day
	• Remoxipride	150-450 mg/day
Dibenzodiazepine	Clozapine	25-900 mg/day
Benzisoxazole	Resperidone	2-16 mg/day

The groups of anti-psychotic drugs differ in their indications for use and side-effects. Clozapine and resperidone have a much lower incidence of extrapyramidal side-effects probably because of their strong blocking effect on serotonin ( $S_2$ ) receptors and relatively weaker dopamine receptors ( $D_2$ ) blockade. Neutropenia and agranulocytosis are serious side-effect i.e. the drug

**Mood-disorders:** These disorders are characterised by the disturbance in the regulation of mood behavior and affect. They are divided into:

1. **Primary affective disorders**

- Unipolar - depression and mania, the recurrences always take either a depressive form (depression) or elation of mood (mania).
- Bipolar - manic-depression. The recurrences are both manic (elation of mood) and depression (depressive mood)

2. **Secondary affective disorders.** They follow another psychiatric (alcoholism, schizophrenia) or physical illness

Treatment of depression requires co-ordination of short-term symptom, remission with long-term continuation and maintenance strategies designed to prevent relapse and recurrence.

## ANTIDEPRESSANTS

There is no ideal anti-depressant: no current compound has rapid onset of action, moderate half-life, low side-effect profile, a meaningful relationship between dose and blood level and minimal interaction with other drug. Therefore, a rational approach to select an anti depressant to use involves knowledge of differences in pharmacokinetic activity and matching of patient preference and medical history with metabolic and side effect profile of the drug considered. About 60 to 70% of all depressed patients respond to any antidepressant drug chosen (Table 3.23) if it is given in a sufficient dose for 6-8 weeks.

Antidepressants should be prescribed in limited quantity at one time as they are dangerous in over dosage. Newer antidepressants (5 HT reuptake inhibitors) are less dangerous as compared to older tricyclics.

**Table 3.23:** Some commonly used antidepressants and side effects

Drug	Usual dose	Adverse effects
A. <b>Tricyclic</b>		
First generation		
Amitriptyline	75-150 mg (<6 yr-10 mg 6>10-20 mg 11-16 yrs: 50 mg)	All produce following side effects <ul style="list-style-type: none"><li>• Sedation (antihistaminic effect).</li><li>• Anticholinergic effects e.g. dry mouth, constipation, urinary hesitancy, blurred vision</li><li>• Extrapyramidal effects e.g. tremors, dystonia, dyskinesia.</li><li>• CVS effects e.g. hypotension, arrhythmias</li><li>• Sexual dysfunction e.g. impotence, impaired ejaculation.</li><li>• Seizures, insomnia</li><li>• Other effects e.g. weight gain, headache, agranulocytosis</li></ul>
Imipramine	75-150 mg (<12 yrs-25 mg)	
Dothiepin	75-150 mg (>12 yrs-50 mg)	
Clomipramine	75-150 mg	
Second-generation		
Amoxapine	150-250 (max 300 mg)	More potent, side effects less Amoxapine carries the risk of tardive dyskinesia; maprotiline may produce seizure.
Trazadone	150-250 mg	
Maprotiline	150-200 mg	
B. <b>Tetracyclic</b>		
• Mianserin	30-60 mg	Cardiovascular and anticholinergic side effects are less.
C. <b>Selective 5 HT reuptake inhibitors (SSRIs)</b>		
Fluoxetine	20-80 mg /day	Not recommended in children
Fluvoxamine	100-200 mg/day	
Sertraline	50-100 mg/day	
Paroxetine	20-50 mg/day	
D. <b>MAO inhibitors</b>		
Phenelzine	60-90 mg/day	300-600 mg/day
Tranylcypromine	20-40 mg/day	
Moclobemide	300-600 mg/day	

Note: Start with the lowest dose and increase it gradually to achieve therapeutic response and then reduce the dose to half as maintenance dose.



It takes about a week or more of continuous treatment for suppression of symptoms. Optimal level of therapy should continue for another week before dose reduction is attempted. Premature withdrawal of medication can lead to recurrences of symptoms. Remission generally occurs after 3-12 months or even longer. Some patients respond to maintenance therapy with half of the therapeutic dose for several months to prevent a relapse. In recurrent depression, prophylactic maintenance therapy may be needed for several years.

Prescribing more than one antidepressant at the same time (polytherapy) is not recommended. Not only it may constitute a hazard but there is no evidence that side-effects are minimized by the combinations.

Mixed preparations of an antidepressant with an anxiolytic are not recommended because individual doses need to be adjusted separately. Besides, antidepressants are given for long duration while anxiolytics are to be prescribed for brief periods.

### Tricyclic Antidepressants

**Action:** They inhibit the re-uptake of amines (noradrenaline and 5-HT) at synaptic clefts and this action has been used to support the hypothesis that affective disorders (e.g. depression) result from a deficiency of these amines which serve as neurotransmitters in the CNS. These are the drug of choice in the treatment of depressive illness. There is a delay of 2 to 3 weeks between the start of treatment and the onset of therapeutic effects.

#### Uses

1. Primary affective disorders such as depression.
2. Secondary affective disorders e.g. depression associated with medical illness.
3. Along with anxiolytic, they are used for agitated depression.
4. Nocturnal enuresis or bed-wetting not due to an organic cause. A single dose at bed time for 6 weeks of either imipramine or amitriptyline is prescribed.
5. Neuropathic pains e.g. trigeminal neuralgia, post-herpetic neuralgia, diabetic neuropathy, etc.

*Dose and Side-effects* Table 3.23.

Tricyclic antidepressants have anticholinergic and extrapyramidal side effects which are less with second generation tricyclics such as trazadone, amoxapine, bupropion, etc.

### Tetracyclic Antidepressants (e.g. mianserin, maprotiline)

They differ structurally and in mechanism of action from tricyclic antidepressants. Mianserin is an  $\alpha_2$ -adreno-receptor antagonist, also inhibits 5-HT uptake (weak effect)

Cardiovascular and anticholinergic effects are markedly reduced. Mianserin has sedatory effect.

### Selective Serotonin Reuptake Inhibitors (SSRIs)

They include: Fluoxetine, Fluvoxamine, Paroxetine and Sertraline).

**Actions:** They are selective inhibitors of 5-HT reuptake producing an increase in the amount of this neurotransmitter at central synapses.

**Side-effects:** They have little or no effect on reuptake of other central neurotransmitters and so are virtually free of noradrenergic and cholinergic side effects. The side effects include; headache, nausea, anorexia, sleep impairment, sexual dysfunction, akathisia (an inner sense of restlessness and anxiety). A serious side effect of concern is **serotonin syndrome** thought to result from hyperstimulation of brain-stem 5-HT<sub>1A</sub> receptors and characterised by myoclonus, agitation, abdominal cramping, hyperpyrexia, hypertension, and potentially death.

#### Drug interactions of SSRI

1. MAO inhibitors. They precipitate serotonin syndrome- an absolute contraindication.
2. Serotonin agonists e.g. tryptophan, fenfluramine
3. Antipsychotics, beta-blockers, calcium-channel blockers, codeine, terfenadine etc.
4. Anticoagulants
5. Quindine

*Dose* See the Table 3.23.

### Monoamine Oxidase Inhibitors (MAO Inhibitors)

They include: Phenelgine, Tranylcypromine

**Actions:** They inhibit the metabolism of noradrenaline and 5-hydroxy-tryptamine (serotonin), hence, increase the availability of these neurotransmitters in CNS.

**Uses**

1. They are less effective than tricyclics for severe depressive illness but are especially effective for milder illness.
2. They are effective particularly when depression is associated with anxiety and phobic symptoms.
3. They are useful in management of primary phobic disorders.

**Side effects:** The common side effects include orthostatic hypotension, weight gain, insomnia, and sexual dysfunction.

### Caution or Drug Interactions

They should not be used with:

- i. Foods rich in tyramine such as cheese, pickled herrings, degraded protein and red wine. There is risk of hypertensive crisis.
- ii. Amphetamines and opiates
- iii. **Dosage:** The dosage of antidepressants are given in the Table 3.23.

### Side Effects of Antidepressants and Their Management

They are given in the Table 3.24. The side effects are mostly dose-related, hence, to be managed with reduction in the dose and measures to relieve symptoms.

### Mood Elevators/Stabilisers

They include:

1. Lithium carbonate: It is used in the treatment of mania and manic-depressive psychoses.
2. Carbamazepine is also effective in mania
3. Sodium valproate is equally effective in acute mania

**Dosage and Side Effects** Table 3.25.

### ANXIOLYTICS AND HYPNOTICS

These drugs relieve anxiety and its related symptoms and some may induce sleep. Anxiolytics include, benzodiazepine, betablockers and azapirone (buspirone).

### Benzodiazepines

These include: chlordiazepoxide, alprazolam, clonazepam, clobazam, diazepam, flurazepam, lorazepam, nitrazepam and oxazepam.

**Actions:** They exert sedative, anxiolytic, muscle relaxant and anticonvulsant actions for which they are used in medicine.

**Table 3.24:** Antidepressants side-effects and their management

Symptoms	Management with special comment
Gastrointestinal e.g. nausea, loss of appetite	Usually short lived. Consider temporary dose reduction or administer with food and antacids
Diarrhoea	Famotidine 20-40 mg/day
Constipation	Wait for tolerance. Diet change, stool softener and exercise. Avoid laxatives
Sexual dysfunction e.g. impotence, impaired ejaculation	<ul style="list-style-type: none"> <li>• Consider drug reduction; drug holiday</li> <li>• Bethanechol, 10-20 mg 2 hr before activity or cyproheptadine 4-8 mg 2 hr before activity or amantadine 100 mg bid/tid.</li> </ul>
Orthostatic hypotension	Tolerance unlikely, increase fluid and salt-intake. Use calf exercises/calf support; flurocortisone 0.025 mg/day.
Anticholinergic e.g. dry mouth, eyes	Wait for tolerance. Maintain good oral hygiene; Use artificial tears, sugar free gum
Tremors	Antiparkinsonian drugs are ineffective. Use dose reduction/slow increase, lorazepam 0.5 mg bid or propranolol 10-20 mg bid.
Insomnia	Schedule all doses for the morning, trazodone 50-100 mg at night
Sedation	Coffee, tea, schedule all dosing for bed time.
Headache	Evaluate diet, stress, other drugs, try dose reduction, amitriptyline 50 mg/day
Weight gain	Decrease carbohydrate, exercise, consider fluoxetine.

**Table 3.25:** Commonly used mood stabilisers

Drug	Dose	Side-effects and other effects
Lithium carbonate	Starting dose 300 mg bid/tid Therapeutic blood level 0.8-1.2 mEq/L	<ul style="list-style-type: none"> <li>Common side-effects - nausea, anorexia, diarrhoea, tremors, thirst, polyuria, fatigue, weight gain</li> <li>acne, neutrophilia, hypothyroidism.</li> <li>Blood levels increased by thiazides, tetracycline, NSAIDs</li> <li>Blood levels decreased by bronchodilators, verapamil and carbonic anhydrase inhibitors</li> <li>Rare side-effects-Neurotoxicity, renal toxicity, cardiotoxicity, hypercalcaemia.</li> </ul>
Carbamazepine	Starting dose; 200 mg/bid Therapeutic blood level: 4-12 mg/ml	Nausea, anorexia, sedation, rash, dizziness, ataxia Rare side effects; hyponatraemia, agranulocytosis, Stevens-Johnson syndrome
Valproic acid	Starting dose; 250 mg tid. Therapeutic blood level: 50-125 mg/ml	Nausea, anorexia, weight gain, Sedation, tremors, rash, alopecia Rare side-effects: Pancreatitis, hepatotoxicity, Stevens-Johnson syndrome

### Uses

1. Chlordiazepoxide, diazepam, lorazepam and oxazepam, all are used in the treatment of anxiety and tension. Alprazolam is used as a day-time tranquilliser. They are also used in phobic disorders, acute stress disorder and post-traumatic stress disorders.
2. Chlordiazepoxide and diazepam are also used in the treatment of muscular spasms e.g. during anaesthesia and in tetanus.
3. Nitrazepam and flurazepam are used as hypnotics for insomnia.
4. Parenteral diazepam is used:
  1. As a muscle relaxant to relieve spasms in tetanus and as premedication during anaesthesia.
  2. Status epilepticus
  3. Convulsions due to various causes
  4. Acute severe anxiety or medical illness
  5. As a sedative for surgical and other procedures
  6. Alcohol withdrawal.

**Dosage:** The dosages of common anxiolytic drug are given in the Box 3.10.

### Side-Effects

1. CNS effects e.g. drowsiness, light headedness, confusion, ataxia, vertigo, drug-dependence.

### Box 3.10: Common anxiolytic drugs

Group	Drug	Usual dose
Benzodiazepines	Diazepam	2-30 mg/day
	Chlordiazepoxide	5-30 mg/day
	Nitroazepam	5-10 mg/day
	Temazepam	10-20 mg at night
Betablocker	Propranolol	20-80 mg/day
Azapirone	Buspirone	10-45 mg/day
<b>Note:</b> <ol style="list-style-type: none"> <li>1. A short course of benzodiazepine is mostly preferred. Administration should be at the lowest dose possible and perscribed on an as-needed basis as symptoms warrant.</li> <li>2. Benzodiazepines should not be prescribed for more than 4-6 weeks because of development of tolerance and the risk of abuse and dependence.</li> </ol>		

2. GI symptoms—nausea, gastric upset
3. Hypotension
4. Visual disturbance
5. Skin rashes
6. Urinary retention
7. Change in libido
8. Rare side effects include blood disorders and jaundice

### Dependence and Withdrawal Symptoms

The benzodiazepines are known to cause dependence and withdrawal symptoms in many patients who have taken them for 6 weeks or more. Withdrawal symptoms occur especially with short-acting benzodiazepines

(alprazolam, oxazepam) and if medication is stopped abruptly, the withdrawal symptoms may appear (listed in the Box 3.11).

**Box 3.11: Benzodiazepine withdrawal symptoms**

- |                                  |                      |
|----------------------------------|----------------------|
| • Anxiety, confusion             | • Hallucinations     |
| • Epileptic seizures             | • Ataxia             |
| • Heightened sensory perceptions | • Paranoid delusions |

### Method of withdrawal

Benzodiazepines withdrawal can be a problem and may be dangerous, hence, they are withdrawn slowly in step-wise fashion i.e one-eight of their daily dose is reduced after every two weeks to prevent withdrawal symptoms. Patients who are taking a benzodiazepine other than diazepam, can be transferred to diazepam in the following manner.

*Step 1:* Transfer to an equivalent dose of diazepam to be taken at night.

Equivalent doses: Approximately 5 mg of diazepam is equal to:

Chlordiazepoxide	15 mg
Alprozolam	0.5-1 mg
Lorazepam	0.5 mg
Nitrozeepam	5 mg
Oxazepam	15 mg
Temazepam	10 mg

*Step 2* Reduce the diazepam dose by 2.5 mg every two weeks. If withdrawal symptoms occur, maintain the dose till symptoms improve.

*Step 3* Reduce the dose further, if necessary in smaller steps. It is better to reduce too slowly than too quickly.

*Step 4* Stop completely. Duration needed to complete withdrawal can take a month or even a year or more.

Betablockers should only be given, if other measures fail.

## DRUGS USED IN GASTROENTEROLOGY

Avoid adrenaline in patients with cardiovascular disease.

### H<sub>2</sub>-Blockers (anti-hypersecretory agents)

#### Action

They block the responses initiated by H<sub>2</sub>-receptors stimulation such as gastric acid output.

#### Preparations

- Cimetidine—Not used now-a-days because of side-effects
- Ranitidine
- Famotidine
- Nizatidine

#### Uses

- Healing of peptic (duodenal) ulcer
- Reflux oesophagitis/gastroesophageal reflux disease
- Zollinger-Ellison's syndrome
- Drug-induced acute gastric erosions
- Fulminant hepatic failure to reduce the incidence of gastric erosions
- Poisoning—corrosive, aluminium phosphide
- Cerebrovascular accidents especially subarachnoid haemorrhage to reduce the incidence of stress induced acute gastric erosions
- Nonspecific dyspepsias or nonulcer dyspepsia.

#### Side Effects

- Dizziness, somnolence, fatigue, confusion and transient rashes
- Liver dysfunction i.e. rise in serum aminotransferases
- Blood—thrombocytopenia and leucopenia
- Hypersensitivity reactions, anaphylaxis
- Breast symptoms such as gynaecomastia is seen with cimetidine, rare with ranitidine

#### Special Precautions

- Famotidine is not recommended for children
- They are not recommended in impaired renal function, pregnancy and lactation

#### Dose

##### Oral

Ranitidine—150 mg bid or 300 mg at bedtime

Famotidine—40 mg at bed time daily or 20 mg bid

Nizatidine—300 mg at bed time daily or 150 mg bid

##### Injections

- Ranitidine 150 mg IV slowly then 150 mg bid I.V infusion 12 hourly depending on the clinical condition

**Table 3.26:** Proton pump inhibitors

Drug	Short-term	Maintenance	Side effects
Omeprazole	20-40 mg once daily	20 mg at night	Hypergastrinemia, diarrhoea, nausea, headache, skin rashes, dizziness, drowsiness, insomnia, myalgia, arthralgia and drug interactions with warfarin, phenytoin
Lansoprazole	30 mg once daily	15 mg at night	Same as above
Pantoprazole	40 mg once daily	Not recommended	Same as above
Esomeprazole	20 mg once daily	do	Side effects are less and it is more potent than others
Rabeprazole	20 mg once daily	do	do

- Famotidine 20 mg I.V slowly over 2 minutes then 20 mg IV infusion 12 hourly depending on the clinical condition

### Proton Pump Inhibitors

Hydrogen ions, accompanied by chloride ions are secreted in response to the activity of  $H^+/K^+$  ATPase (proton pump) from the parietal cell membrane of gastric mucosa. The proton pump is the final step in production of gastric acid.

### Actions

These are benzimidazole compounds that specifically and irreversibly inhibit proton pump ( $H^+/K^+$  ATPase inhibitors) action and are most powerful inhibitors of gastric acid secretion. The maximum inhibition occurs within 3-6 hours after an oral dose.

*Preparations and Doses Table 3.26.*

### Uses

- NSAIDs and aspirin-induced acute gastric erosions
- Duodenal and gastric ulcers. In *duodenal ulcer*, it is used for eradication of *H. pylori* and to promote healing of the ulcer
- Reflux oesophagitis or gastrointestinal reflux disease
- Zollinger-Ellison's syndrome

### Contraindications

- Pregnancy and lactation
- Not recommended for children

### *H. pylori* Infections

- The conditions associated with *H. pylori* infection are given in Box 3.12.

#### **Box 3.12:** Clinical association of *H. pylori* infections

- Duodenal ulcer—Strong association
- Gastric ulcer—Strong association
- Gastric cancer—Less common association
- Gastric  $\beta$ -cell lymphoma—Less common association

### Diagnosis of *H. pylori* Infection (Table 3.27)

**Table 3.27:** Diagnostic methods of *H. pylori* infection

- Noninvasive tests**
  - Serology*: Kits are available. The test lacks sensitivity and specificity, hence, is good for population studies
  - Urea breath test*. It has high sensitivity and specificity but is costly
- Invasive methods (Gastric biopsy)**
  - Histology*. It is sensitive, specific and cheap but it takes several days to process. False negatives occur
  - Rapid urease test*. It is cheap, quick and specific but is less sensitive
  - Microbial culture*. It is gold standard for diagnosis. It is laborious procedure

### Eradication of *H. pylori*

The antibiotic regimen is given in Table 3.28.

### Anticholinergics (cholinergic receptors blocking agents)

#### Definition

Anticholinergics inhibit parasympathomimetic action with the result that;



**Table 3.28:** Antibiotic regimens for *H. pylori* eradication

<b>1. Triple Drug Regimens</b>			
First line		Second line	
OCM/LCM	OAC/LAC	OAM/LAM	BAM
<ul style="list-style-type: none"> <li>Omeprazole 40 mg OD or Lansprazole 30 mg 12 hourly plus</li> <li>Clarithromycin 500 mg 12 hourly plus</li> <li>Metronidazole 400 mg 12 hourly</li> </ul>	<ul style="list-style-type: none"> <li>Omeprazole 40 mg OD or Lansprazole 30 mg 12 hourly plus</li> <li>Amoxicillin 500 mg 12 hourly plus</li> <li>Clarithromycin 500 mg 12 hourly</li> </ul>	<ul style="list-style-type: none"> <li>Omeprazole 40 mg OD or Lansprazole 30 mg 12 hourly plus</li> <li>Amoxicillin 500 mg 12 hourly plus</li> <li>Metronidazole 400 mg 12 hourly</li> </ul>	<ul style="list-style-type: none"> <li>Bismuth (CBS) 125 mg 6 hourly plus</li> <li>Amoxicillin 500 mg 12 hourly plus</li> <li>Metronidazole 400 mg 12 hourly</li> </ul>
"Triple Regimen"	"Triple drug Regimen"	"Triple drug Regimen"	"Triple drug Regimen"
Duration 7 days	7 days	7-10 days	14 days
Efficacy 90%	90%	85%	80%
<b>2. Dual Drug Regimen</b>			
<ul style="list-style-type: none"> <li>Omeprazole 40 mg OD plus</li> <li>Clarithromycin 500 mg tid</li> </ul>	For two weeks. It is less effective but more costly		

- They reduce secretion and motility of the stomach and intestines
- They increase heart rate and enhance atrio-ventricular conduction
- They reverse cholinergic-mediated bronchoconstriction and diminish respiratory tract secretions

#### Preparations

These include: *Dicyclomine*, *ambutonium*, *atropine*, *belladonna alkaloids*, *glycopyrronium*, *hyocine*, *hyoscyamine*, *isopropamide*, *mepenzolate*, *pipenzolate*, *piperidolate*, *poidine*, *clidinium* and *ipratropium* etc.

#### Uses

They are used as;

- Antispasmodics to relieve gripping pain by smooth muscle relaxation
- Antidiarrhoeal agents to reduce motility
- Anti-peptic ulcer medication
- Irritable bowel syndrome to relieve spasms
- Atropine is used in complete heart block and OP compounds poisoning (read atropine).

#### Side-effects

Dry mouth, thirst, dizziness, fatigue, sedation, blurred vision, rash, constipation, loss of appetite, nausea, headache, urinary retention and tachycardia.

#### Contraindications

- Glaucoma
- Obstructive disease of GI tract and intestinal atony or paralytic ileus
- Obstructive uropathy
- Myasthenia gravis
- Toxic megacolon in ulcerative colitis
- Hiatus hernia associated with reflux oesophagitis

#### Special Precautions

They are to be used carefully in;

- Pregnancy and lactation
- Prostatic enlargement
- Pyloric stenosis
- Autonomic neuropathy
- Hyperthyroidism
- Children
- Where tachycardia is undesirable
- Elderly patients

*Dosage**Oral*

- *Oxyphenonium bromide* 5-10 mg 4 times a day
- *Dicyclomine* (10 mg tab) 10-20 mg 4 times a day
- *Propantheline* (15 mg tab) 15 mg 3 times a day before meals and 30 mg (2 tab) at night
- *Hyoscine* (10 mg tab) 20 mg 4 times a day  
*children above 6 years*  
10 mg three times a day

*Parenteral*

- *Inj hyoscine* (20 mg/ml) 20-40 mg (IM, SC and IV) 3 or 4 times a day
  - *Inj atropine* (0.6 mg/ml) 1-2 mg IV Dose depends on clinical situations (Table 3.29)
- Inhalation*
- *Ipratropium* (Table 3.29)

**Atropine and its Congeners/Derivatives***Actions and Uses*

1. Atropine blocks muscarinic cholinergic receptors, with little effect on cholinergic transmission at the autonomic ganglia and neuromuscular junctions, hence, CNS effects of atropine or atropine-like drugs are due to blockade of muscarinic synapses. Because of this action, it is used in treatment of organophosphorous poisoning.
2. Atropine increases heart rate and enhances atrio-ventricular conduction. Because of these actions, it may be useful in combating sinus bradycardia or heart block associated with increase vagal tone (vagolytic effect).

3. Atropine reverses cholinergically mediated bronchoconstriction and diminishes respiratory tract secretions. Because of these actions;
  - i. It is used as pre-anaesthetic medication.
  - ii. Its congener ipratropium is used in acute severe asthma by inhalation (inhalor)
4. It decreases GI motility and secretion. Because of these actions its various derivatives and congeners such as propantheline, isopropamide and glycopyrrrolates are used in patients with peptic ulcer and diarrhoeal syndromes/diseases.
5. Anticholinergics or atropine like drugs, e.g. benzhexol, benztropine, orphenadrine, procyclidine are used in the treatment of parkinsonism and drug-induced extrapyramidal disorders (read antiparkinsonism drugs).

**Anticholinesterase Agents or Acetylcholinesterase Inhibitors**

Acetylcholine is a neurotransmitter at the autonomic ganglia, at the postganglionic parasympathetic nerve endings, at the postganglionic sympathetic nerve endings innervating the sweat glands, and at the skeletal muscle end plate (neuromuscular junction).

Anticholinesterase causes hydrolysis of acetylcholine and inactivates the neurotransmitter at cholinergic synapses. This enzyme is present as true cholinesterase within neurons and is distinct from pseudocholinesterase present in plasma and nonneuronal tissue. The pharmacological effects of anticholinesterase agents

**Table 3.29:** Cholinergic receptors blocking agents

Agent	Indication	Dose and route	Comment
1. Atropine	<ul style="list-style-type: none"> <li>• Bradycardia and hypotension</li> <li>• Heart block</li> <li>• Organophosphorous poisoning</li> </ul>	0.4-1.0 mg I.V 1-2 hours  1-2 mg stat then oral propantheline 15 mg tid 1-2.0 mg every 5-10 min till the signs of atropinsation (dry mouth, mid-dilated pupil and increase in heart rate) appear, then slowly reduce the dose and withdraw it over a period of 5-7 days	Competitive inhibition of $M_1$ and $M_2$ receptor; blocks haemodynamic changes associated with increased vagal tone  <ul style="list-style-type: none"> <li>• Competitive inhibition of muscarinic receptors</li> </ul>
2. Ipratropium	<ul style="list-style-type: none"> <li>• Asthma</li> <li>• COPD</li> </ul>	500 mg by inhalation (nebulizer) tid or qid	Anticholinergic bronchodilator

**Table 3.30:** Anticholinesterase agents—doses and indications

Agent	Indication	Dose and route	Comment
Physostigmine	<ul style="list-style-type: none"> <li>Treatment of myasthenia gravis</li> </ul>	Oral 60 mg 3 to 5 times daily	<ul style="list-style-type: none"> <li>Action begins within 15-30 minutes and lasts for 4 hours</li> <li>At least partial improvement in most myasthenic patients although improvement is complete in few patients</li> </ul>
	<ul style="list-style-type: none"> <li>Central cholinergic blockade produced by overdose of atropine and tricyclic antidepressants</li> </ul>	IV 1-2 mg slowly	<ul style="list-style-type: none"> <li>Tertiary amine; penetrates the CNS well and may cause seizure</li> </ul>
Edrophonium	Paroxysmal supraventricular tachycardia	5 mg IV (after 1.0 mg of test dose)	<ul style="list-style-type: none"> <li>Induces vagotonic response, rapid onset, short duration of action; effects reversed by atropine</li> </ul>
Neostigmine	<ul style="list-style-type: none"> <li>Myasthenia gravis treatment</li> <li>Central neuromuscular blockade</li> </ul>	Oral: 15-30 mg at suitable intervals through out the day (Total dose 75-300 mg) Children < 6 yr initial dose 7.5 mg > 6 yr initial dose 15 mg Parenteral (SC or IM) 1 to 2.5 mg at suitable interval throughout the day (Usual dose 5-20 mg) IM or SC at a dose of of 1 to 2.5 mg	<ul style="list-style-type: none"> <li>It is quarternary amine, does not penetrate CNS</li> <li>It is contraindicated in intestinal and urinary obstruction</li> </ul>
	<ul style="list-style-type: none"> <li>Postoperative intestinal atony</li> <li>Urinary retention</li> </ul>	IM or SC at a dose of 1 to 2.5 mg	

are due to inhibition of neuronal (true) acetylcholinesterase.

#### Actions and Uses

Acetylcholinesterase (cholinesterase) inhibitors enhance the effects of parasympathetic stimulation by diminishing the inactivation of acetylcholine (ACh). They are used;

- In treatment of myasthenia gravis.
- Termination of neuromuscular blockade following general anaesthesia.
- Reversal of intoxication produced by agents having central anticholinergic action e.g. atropine.
- Cholinesterase inhibitors induce a vagotonic response in the heart and may be useful in terminating attacks of paroxysmal supraventricular tachycardia.

#### Contraindications

- Intestinal and urinary obstruction.

#### Special Precautions

- Asthma, bradycardia, recent MI, epilepsy, hypotension, Parkinsonism, vagotonia, peptic ulcer, pregnancy and lactation.

#### Side Effects

- Nausea, vomiting, diarrhoea, increased salivation and abdominal cramps.

**Dosage** See the Table 3.30.

#### Signs of Overdose

- GI discomfort increased bronchial secretions sweating, involuntary defecation and micturition, miosis, nystagmus, bradycardia, agitation, hypotension, fasciculations and paralysis.

**Dopamine Antagonist***Drugs*

- Phenothiazines (oral and parenteral)
- Metoclopramide (oral and parenteral)
- Domperidone (oral)

*Actions and Uses*

1. *Anti-emetic*: Dopamine antagonists suppress proemetic stimuli by blocking D<sub>2</sub> receptors in chemoreceptor trigger zone. They are useful in relieving nausea and vomiting due to variety of conditions including those due to cytotoxic drugs. They are used prophylactically to prevent post-operative vomiting.
2. *Prokinetic effect*: Due to reduction in motility and increasing the tone of lower oesophageal sphincter, they are used for treatment of reflux oesophagitis or gastro-oesophageal reflux disease and gastritis.
3. They are also used for *hyperacidity, nonulcer dyspepsia, hiatus hernia* and *hic-cups*.

*Side Effects*

- *Extrapyramidal reactions*, e.g. dystonia and tardive dyskinesia, parkinsonism
- *CNS*—depression, restlessness, drowsiness neuroleptic malignant syndrome
- *Raised serum prolactin levels* e.g. galactorrhoea in nonlactating mothers.

*Contraindications*

- Phaeochromocytoma and recent GI surgery

*Dose*

10 mg two or three times daily orally or parenterally.

*Prokinetic Agents**Actions*

- They facilitate or restore gastrointestinal motility by indirectly enhancing acetylcholine release from myenteric plexus
- They increase the tone of the lower oesophageal sphincter
- They reduce gastric acid secretion also

*Uses*

- Gastro-oesophageal reflux disease (GERD)
- Constipation (chronic)
- Gastroparesis associated with diabetes, systemic sclerosis and autonomic neuropathy.

*Contraindications*

- Not recommended for children
- Personal or family history of prolonged QT or ventricular arrhythmias, irregular heart beats or abnormal ECG and marked bradycardia
- Persistent vomiting or dehydration
- Pregnancy
- GI haemorrhage, obstruction or perforation
- Hypokalaemia or hypomagnesaemia

*Side Effects*

- *GI symptoms*—abdominal cramps, borborygmi, diarrhoea
- *CNS symptoms*—headache, extrapyramidal effects, convulsions
- *Urinary*—increased urinary frequency
- *Cardiac*—arrhythmias
- *Liver function abnormalities*
- *Hyperprolactinaemia*.

*Preparation and Dosage*

- *Cisapride*—It is a banned drug due to potential arrhythmogenic effect
- *Mosapride*—10 mg 3-4 times a day orally
- *Itopride*—10 mg 2-3 times a day.

**HORMONES****CALCIUM AND PARATHARMONE**

Normal adult plasma calcium level is 2.2 to 2.6 mmol/L (9 to 10.5 mg%) and ionised calcium is 1.1-1.4 mmol/L (4.5-5.6 mg%)

The calcium in plasma is present in three forms i.e. *unbound or free calcium ions* (ionised calcium), *bound calcium* (ions bound to plasma proteins) and *diffusible complexes*. The concentration of ionised calcium influences many cellular functions (neuromuscular) and

is subjected to tight hormonal control especially through parathormone (PTH).

#### Precautions

Never take the blood sample for calcium with the help of tourniquet or by manual compression of arm.

It is ionised calcium which is significant clinically hence, it should be measured by calcium specific electrodes.

If ionised calcium cannot be measured, then protein bound fraction can be calculated as follows

$$\% \text{ protein bound Ca} = 0.8 \times \text{albumin (g/L)} + 0.2 \times \text{globulin (g/L)} + 3$$

By subtracting protein bound calcium from total calcium, one can calculate ionised calcium (approx).

#### Caution

The serum calcium should not be interpreted in isolation but with concentration of serum proteins which is an important determinant for which correction may be sometimes necessary. The correction is "Add 1 mg/dl to the serum calcium level for every 1g/dl fall in the serum albumin level below 4 g/dl. For example, if serum calcium is 7.8 mg% but serum albumin is 3 g/dl then stated serum calcium (corrected) will be  $7.8 + 1 = 8.8$  mg/dl which is within normal range".

### Hypocalcaemia

Chronic hypocalcaemia characterised by neuromuscular irritability and neuropsychiatric manifestations such as paraesthesias, numbness (circumoral), cramps, tetany, convulsions, laryngeal stridor and psychosis results from a variety of causes (Box 3.13).

### Tetany

#### Definition

This is a clinical condition characterised by low levels of ionised calcium ( $<4.8$  mg%) leading to increased neuromuscular excitability. In this condition, total levels of calcium may even remain normal.

**Latent tetany:** Two clinical signs are helpful in latent tetany.

#### Box 3.13: Causes of hypocalcaemia

##### 1. Increased phosphate levels

- Chronic renal failure
- Phosphate therapy

##### 2. Drugs

- Calcitonin
- Diphosphonates

##### 3. Hypoparathyroidism (Congenital or acquired)

- Congenital deficiency e.g. DiGeorge's syndrome (intellectual impairment, cataract, calcification of basal ganglia, congenital cardiac and developmental defects, impaired immune response)
- Idiopathic (autoimmune) hypoparathyroidism
- Following neck exploration e.g. thyroidectomy, parathyroidectomy

##### 4. Resistance to parathormone (PTH)

- Pseudohypoparathyroidism

##### 5. Vitamin D related

- Vitamin D deficiency
- Resistance to Vit. D

##### 6. Miscellaneous

- Acute pancreatitis
- Citrated blood transfusions

**Trousseau's sign:** The inflation of the sphygmomanometer cuff above diastolic blood pressure or 100 mm of Hg for 3 minutes induces tetanic spasms of fingers and wrist.

**Chvostek's sign:** Tapping over facial nerve near stylo-mastoid foramen results in twitching of facial muscles.

*Causes (see the Box 3.14)*

For neuromuscular function, calcium, potassium and magnesium are essential, hence, low levels of these cations lead to tetany. Alkalosis leads to tetany while acidosis prevents it.

#### Box 3.14: Causes of tetany

##### Hypocalcaemic

- Malabsorption
- Osteomalacia
- Acute pancreatitis
- CRF
- Anticonvulsants e.g. dilantin

##### Alkalotic and hypokalaemic

- Repeated vomiting
- Excessive intake of alkalis
- Hysterical hyperventilation
- Primary hyperaldosteronism
- Acute anionload (e.g. citrate, lactate,  $\text{HCO}_3$ )

##### Hypomagnesemic

- Idiopathic



Indications of parenteral calcium gluconate and chloride

### 1. Calcium gluconate

- Tetany due to any cause
- Hyperkalaemia
- Hypermagnesaemia
- Acute hypoparathyroidism
- Pseudohypoparathyroidism

2. **Calcium chloride** is used in cardiac arrest and aluminium phosphide intoxications

## ANTI-DIABETIC AGENTS

### Oral Hypoglycaemics (OHA)

Classification: They are classified into two groups;

1. *Insulin secretagogues (they stimulate insulin secretion by  $\beta$ -cells of pancreas)*

#### A. Sulfonylureas

- First generation:* Chlorpropamide, tolbutamide, Acetohexamide, Tolazamide
- Second generation:* Glibenclamide, glipizide, gliclazide, glimepiride

#### B. Nonsulfonylureas

- Meglitinide derivative-Repaglinide, Nateglinide.

### 2. Insulin Sensitizers

- Biguanides e.g. metformin, phenformin
- Thiazolidinediones derivatives e.g. rosiglitazone, pioglitazone
- Anti-obesity drugs
- Chromium piconitate

### 3. Inhibitors of carbohydrate absorption ( $\alpha$ -glucosidase inhibitors)

- Acarbose, miglitol, voglibose

### 4. Miscellaneous

- Glucagon like peptide-I
- Guar gum
- Vanadium salts

### Sulphonylureas

Mechanisms of Action

- Pancreatic:* They stimulate  $\beta$ -cells of the pancreas by binding to receptors i.e. sulphonylurea receptors.

- Extrapankreatic:* This effect includes an increase in the number of insulin receptors and enhancing the insulin-mediated glucose transport independent of increased insulin binding (pancreatic effect).

### Indications of Sulphonylureas

1. Monotherapy: Type 2 diabetes (NIDDM)—Nonobese patients not controlled on diet and exercise are candidates for monotherapy.
2. Combination therapy: They can be used in obese type 2 diabetics not controlled on diet, exercise and maximum dose of metformin (a biguanide)
3. Other uses: Chlorpropamide is useful in the treatment of patients of diabetes insipidus as it sensitizes the renal tubule to antidiuretic hormone [ADH].
4. Repaglinide or nateglinide has also been used for control of postprandial hyperglycaemia.

Dosage (Box 3.15)

Contraindications

- Type I diabetes
- Metabolic decompensation with acidosis

**Box 3.15:** Oral hypoglycaemic agents (OHA)

Agent	Usual daily dose (mg)	Doses per day	Duration of action in hours
<i>First generation drugs</i>			
Acetohexamide	200-500	1-2	12-18
Chlorpropamide	100-500	1	60
Tolbutamide	500-3000	2-3	6-12
Tolazamide	100-1000	1-2	12-14
<i>Second generation drugs</i>			
Glibenclamide	2.5-20	1-2	12-24
Glipizide	2.5-30	2-3	6-12
Gliclazide	40-320	1-2	12-24
Glimepiride	1-6 mg	1	upto 24
<i>Meglitinide</i>			
Repaglinide	1-4	1	upto 24
Nateglinide	30-60	1	upto 24 hr
<i>Biguanides</i>			
Metformin	1500-3000	1-2	upto 24
<i>Thiazolidinediones derivatives</i>			
Rosiglitazone	2-8	1	upto 24
Pioglitazone	15-45	1	upto 24

- Diabetic coma or precoma
- Renal or hepatic insufficiency
- Pregnancy
- Patients exposed to unusual stress
- Hypersensitivity to sulphonamides

*Note:* The contraindications of OHA are actually indications of insulin.

### **Nonsulfonylureas (e.g. repaglinide, nateglinide)**

#### *Action*

- They have action similar to sulfonylurea

#### *Uses*

- They are used as an alternative to sulfonylurea.
- In addition they are useful as a monotherapy or polytherapy for control of postprandial hyperglycaemia.

#### *Side Effects*

They include, hypoglycaemia, weight gain, nausea, diarrhoea, skin reactions, paraesthesias, cholestatic jaundice, blood dyscrasias and dilutional hyponatremia.

### **Insulin Sensitizers**

It includes: biguanides and thiazolidinedione derivatives e.g. rosiglitazone, pioglitazone

*Actions:* Recently, it has been proposed that the insulin resistance—a characteristic feature of type 2 diabetes is due to insulin receptors.

Proliferative Peroxime Activating Receptors gamma (PPAR- $\gamma$ ) are associated with obesity and insulin resistance. Insulin sensitizers (metformin and thiazolidinedione derivatives-rosiglitazone and pioglitazone) act by stimulating these receptors and overcome insulin resistance and hyperglycaemia of obese diabetics. By sensitizing the receptors to insulin, they cause peripheral utilisation of glucose in peripheral tissues. Both these sensitizers differ slightly in their site of actions i.e. metformin inhibits hepatic output of glucose more than peripheral utilisation; while thiazolidinedione derivatives are more specific to increase peripheral utilisation of glucose than hepatic output. Due to their different site of actions, they can now be combined for obese type 2

diabetes not controlled with either. In addition, they improve the lipid profile of diabetics.

#### *Indications of biguanides*

1. Monotherapy: They are used in obese type 2 diabetics not controlled on diet and exercise
2. Combination therapy: They can be combined with sulphonylurea or thiazolidinedione derivatives if type 2 obese diabetic is not controlled on maximum doses of metformin. It can be used with insulin.
3. Other uses: Metformin is used as antiobesity drug due to its anorectic effect (appetite killer)
4. They are used to lower blood sugar in patients with impaired glucose tolerance (IGT) to prevent diabetes.

#### *Side effects of biguanides*

Nausea, vomiting, anorexia, diarrhoea, metallic taste, weakness and rashes. Lactic acidosis occurs with metformin but infrequently. Hypoglycaemia does not occur with either of them.

### **Thiazolidinedione Derivatives**

*Actions.* They stimulate PPAR- $\gamma$  receptors as described above, thus, increase the peripheral utilisation of glucose in the tissues. They need the presence of insulin for their action.

#### *Uses*

- Monotherapy in type 2 diabetes
- Combination therapy. They can be combined with sulphonylurea or metformin if type 2 diabetes is not controlled with either of them.
- They are used to overcome insulin resistance in polycystic ovarian syndrome
- They can be used in patients with IGT to prevent diabetes.

*Side effects of thiazolidinediones:* upper respiratory symptoms, headache, light headedness, GI symptoms, weight gain, weakness, oedema and occasionally hypoglycaemia.

#### *Contraindications*

1. Old age >65 years

**Box 3.16:** Physiological actions of insulin

Metabolism	Actions	
	Stimulation	Inhibition
Carbohydrates	<ul style="list-style-type: none"> <li>• Uptake of glucose by peripheral tissues</li> <li>• Glucogenesis and glycolysis</li> <li>• Phosphorylation of glucose</li> </ul>	Gluconeogenesis and glycogenolysis
Lipids	Triglyceride and fatty acid synthesis	• Lipolysis and ketogenesis
Proteins	Protein synthesis and aminoacid transport	• Protein degradation
Potassium (K <sup>+</sup> )	Cellular uptake of potassium	—

2. In the presence of renal insufficiency, hepatic insufficiency, cardiovascular disease, pulmonary embolism, tissue hypoxia, pancreatitis, excessive alcohol intake or concomitant use of diuretics.

## Insulins

### Actions of Insulin (Box 3.16)

#### Insulin Preparations

Insulin preparations contain either bovine, porcine or human insulin. Bovine and porcine insulins are obtained from the pancreas of cattle and pigs respectively, both these insulins are unpurified (contain contaminants >10 parts per million) and antigenic in nature, and may lead to complications. Purification of insulin is done to reduce the level of contaminants to less than 10 parts per million. This purification greatly reduces the antigenicity of the products. In this respect, it must be remembered that bovine insulin which differs from human insulin in their aminoacids, is inherently more antigenic than porcine insulin which differ from human by only one aminoacid.

Human insulin is obtained by either enzymatically replacing alanine with threonine in the porcine insulin molecule or by recombinant DNA techniques using bacteria *E.Coli*. Both processes produce a molecule which is identical to human insulin. These insulins are less immunogenic (antigenic), hence insulin complications such as lipodystrophy, allergic reactions or acquired insulin resistance which were seen with unpurified insulin has virtually been abolished.

**Table 3.31:** Main human (purified) insulins and their duration of action

Insulin	Duration of action (hrs)
I. Unmodified	Action starts-within half an hour
A: Rapid/short acting (neurtal or acid soluble)	Peak- 2-3 hrs Duration-6 hrs
• Actrapid*	
• Nordisulin*	
• Humulin-S**	
II. Modified (Depot) (Cloudy solution, contain protamine in isophane or NPH and Zn <sup>++</sup> in Lente prep)	Action starts 1-4 hrs Duration-upto 12-36 hrs
A. Intermediate Acting	12 hrs (approx)
• Monotard*	
• Insulatard*	
• Humulin-I**	
B. Long Acting	24-36 hrs
• Ultratard*	
• Humilin Zn*	
• Humulin-U**	> 36 hrs
III. Biphasic-Acting (stable premixed preparation containing fixed proportions of soluble (rapid acting) and Isophane (intermediate acting) insulin such as 10:90, 20:80, 30:70, 40:60, 50:50.	Action starts within half an hour, reaches its peak at 4-6 hr and remains upto 12 hr
• Mixtard 30:70	
• Humulin 30:70	
IV. Insulin analogues	
• Insulin lispro	3-5
• Insulin aspart	3-5
• Insulin galargin	24
In India, insulins are available in 40 units per ml in 10 ml vials; in USA and Britain, they are available as single strength i.e. 100 units/ml.	
*Manufactured by Novo-Nordisk	
**Manufactured by Eli-Lilly	

### Classification of Insulin

The insulins are classified according to there mode of action irrespective of origin of insulin. They are listed in the Table 3.31.

Now-a-day human insulins are manufactured by recombinant DNA technology

### Indications of Insulin

1. Type I diabetes (IDDM)-An absolute indication.

2. Diabetic ketoacidosis or hyperosmolar non-ketotic coma
3. Types 2 diabetes (NIDDM) with primary or secondary sulfonylurea failure in nonobese persons.
4. Type 2 obese diabetics not responding to maximal doses of sulfonylurea, metformin and thiazolidinediones derivatives.
5. Gestational diabetes or diabetes with pregnancy.  
In this case, only purified, soluble human insulin is used for bringing round-the-clock normoglycaemia or near normoglycaemia.
6. Type 2 diabetics undergoing surgery, having complications, stress or acute infections or not controlled on OHA (Fig. 3.2).
7. *Non-diabetic indications*
  - Insulin with glucose therapy is useful for treatment of hyperkalaemia/hypermagnesaemia
  - Insulin-induced hypoglycaemia is a test for GH secretion.
  - To prevent acute glucotoxicity post-operatively, neutralisation of glucose is done by insulin.

#### Side-Effects

1. *Hypoglycaemia*. This is main side-effect of all types of insulins; the Somogyi effect and *Dawn phenomenon* may occur (Table 3.32).
2. *Lipodystrophy (tumefaction) at the site of injection*. To prevent this, site of injection of insulin should be changed frequently so that same area is not used more than once a month.
3. *Weight gain*.
4. *Insulin resistance*. It is defined as insulin requirement >200 units/day. It is due to anti-insulin antibodies. It is not seen now-a-days with purified insulins.

#### 5. Allergic reactions

The last two side-effects are not seen usually with purified insulins as they are less immunogenic.

#### The Somogyi effect and Dawn Phenomenons

These two phenomena may be seen in patients receiving insulin, more common in children than adults. The differences are given in the Table 3.32.

**Warning:** Do not jump to increase the night dose of insulin on finding high levels of fasting blood sugar in patients who were previously controlled on the same dose of insulin because it could be due to either of two phenomenons and insulin is useful in one and dangerous in other. To differentiate between the two an early morning sample for blood sugar at 3 AM may be taken. The low value indicates Somogyi phenomenon while high value indicates Dawn phenomenon.

#### Regimens of Insulin Therapy

1. *Conventional*: single injections with each major meal(s). This is called two-dose or three dose regimen.
2. *Multiple subcutaneous injection of soluble insulin* in gestational diabetes.
3. *Continuous subcutaneous insulin by insulin delivery device such as insulin pump or pen injector*. This is given in educated and motivated patients who do not have visual impairment, can learn and practise the technique. It is easy, convenient, can be used in public places or restaurants or when patient is on tour or travel. This regimen can be used to treat diabetic ketoacidosis with soluble insulin.

**Table 3.32:** Distinction between Somogyi effect and Dawn phenomenon

Somogyi effect	Dawn phenomenon
<ul style="list-style-type: none"> <li>• Early hypoglycaemia followed by rebound hyperglycaemia (Hypoglycaemia begets hyperglycaemia)</li> <li>• It is due to excess of night dose of insulin.</li> <li>• Early morning symptoms of hypoglycaemia</li> <li>• It is due to counter-regulatory hormones mechanism e.g. release of glucagon, epinephrine and norepinephrine, cortisol and GH</li> <li>• It is abolished by reducing night dose of insulin</li> </ul>	<p>Early hyperglycaemia which is not rebound phenomenon</p> <p>It is due to insufficient night dose.</p> <p>Early morning symptoms of hyperglycaemia</p> <p>It is due to nocturnal release of GH and increased insulin clearance in early morning hours</p> <ul style="list-style-type: none"> <li>• It requires an increase in night dose of insulin</li> </ul>

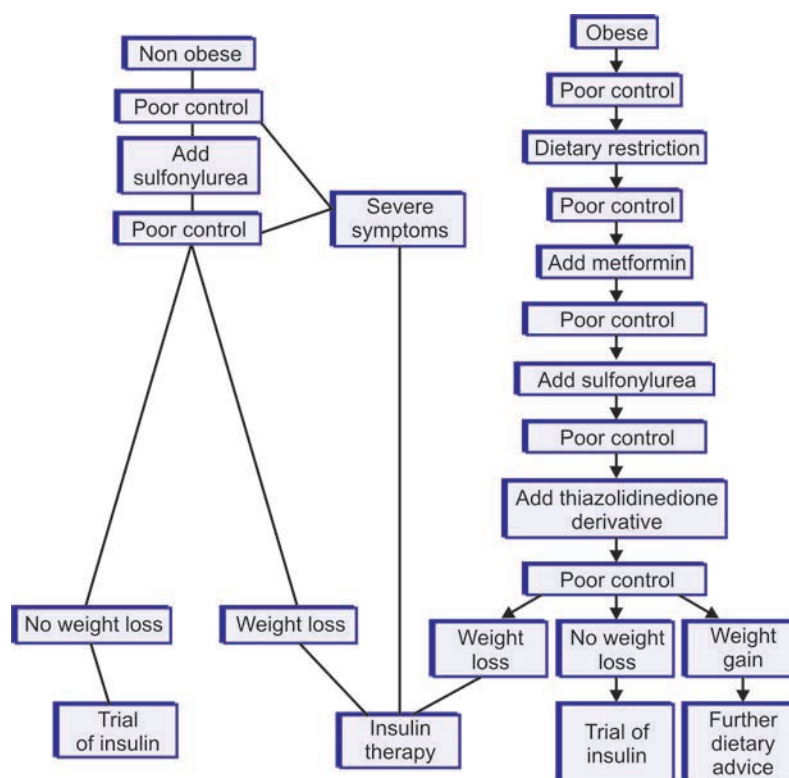


Fig. 3.2: Use of Insulin in Type 2 diabetes mellitus

**Box 3.17: Insulin dose and dosing schedule**

Total dose calculation = 0.5-1.0 U/kg/day			
<b>1. Two-dose regimen</b>			
Type of Insulin	Dose and Frequency distribution		
	Pre-breakfast	Pre-dinner	
Insulin combination such as mixtard (30:70)	2/3 rd of total dose	1/3 rd of total dose	
<b>2. Three-dose regimen</b>			
Insulin	Pre-breakfast	Pre-lunch	Pre-dinner
Type	Plain	Plain	NPH or Lente
Percentage (%) of total dose	25%	15%	60%
<b>3. Multiple dose</b>			
Type of insulin	Lispro	Lispro	Galargine

Calculation of Insulin dose and dosing schedule (Box 3.17).

#### Assessment of Metabolic Control

- Urine estimation for sugar
- Self-monitoring of blood glucose e.g. fasting and postprandial
- Glycosylated Hb (HbA1c or HbA1c) It is done quarterly in all patients. It is formed by nonenzymatic glycation of aminoacids of  $\beta$ -chain of Hb. It gives assessment



of control of preceding 3 months. The values of HbA1c is more reliable and 1-1.5% lower than HbA1. Normal value of HbA1c is <6%.

There is close relationship between metabolic control and the incidence of vascular complications. The results of DCCT and UKPDS trials have concluded that diabetic complications are preventable and can be delayed with tight control (near normal glycaemia). The targets of assessment defined in various studies is to keep HbA1c < 7% to prevent or delay the complications. The criteria recommended by European NIDDM Policy Group (Box 3.18) are Valid and well accepted.

**Box 3.18: European NIDDM Policy Group**  
Target for control of DM

Parameter	Good	Acceptable	Poor
Blood sugar (mg/dl)			
Fasting	80-120	<140	>140
Postprandial	80-160	<180	>180
HbA1% (HbA1c%)	<8.5(<6.5)	8.5-9.5(<7.5)	>9.5(>8.5)
Urine glucose (%)	0	<0.5	>0.5
Total cholesterol (mg%)	200	<250	>250
HDL Cholesterol (mg/dl)	40	>35	<35
Triglyceride (mg/dl)	150	<200	>200
Note: Value of HbA1c is lower i.e. <6% is normal, value between 6.0-6.5, 6.5-7.5 and 7.5-8.5% indicate excellent, good and fair control respectively. Values >8.5% indicate poor control.			

## Antithyroid Drugs

### Actions

These drugs block the synthesis of thyroid hormones in the thyroid gland. Propylthiouracil in addition also decreases peripheral conversion of thyroxine ( $T_4$ ) to triiodothyronine ( $T_3$ ), i.e. a betablock effect.

### Drugs

1. *Carbimazole* is a commonly used drug, methimazole is its active metabolite. The period of treatment, dose schedule and side-effects are given in Table 3.33.
2. *Propylthiouracil*. It is used in patients who are sensitive to carbimazole. It is more potent but dosage is 10 times higher than carbimazole. It is drug of choice for patients of thyrotoxicosis with pregnancy.
3. *Potassium Iodide*. It is not routinely used drug. It is indicated in hyperthyroidism to decrease vascularity in patients before undergoing surgery. It is helpful to control thyroid crisis or storm as an adjuvant to other drugs, hence, used in the emergency situation.
4. *Betablockers*. A nonselective betablocker (propranolol 120-160 mg/day or metoprolol 50 mg/day) is used for symptomatic relief. They prevent the conversion of  $T_4$  to  $T_3$  in peripheral tissue. They are used;
  - i. Along with antithyroid drugs during initial period of 2-3 weeks.

**Table 3.33:** Two commonly employed antithyroid drugs with their dose and duration in thyrotoxicosis

Period	Drug and dosage	Purpose
1. Initial (0-3 weeks)	High dose • Carbimazole (15-20 mg 8 hourly or 1 mg/kg/day in divided dosage) • Propylthiouracil-150-300 mg every 8 hourly	To overcome the thyroid overactivity
2. Later on (4-8 weeks)	Moderate dose: Carbimazole 10 mg 8 hourly or propylthiouracil 150 mg 8 hourly	To bring euthyroid state
3. Lastly (12-24 months)	Maintenance dose: Carbimazole 5-20 mg/day or propylthiouracil 150 mg/day	To maintain normal $T_3$ , $T_4$ , TSH levels

### 334 Bedside Medicine

- ii. Following  $^{131}\text{I}$  treatment. It is used for short period.
- iii. During preparation of patient for surgery.
- iv. For transient thyrotoxicosis during thyroiditis.

#### Indications of antithyroid drugs

- i. Initial treatment of all hyperthyroid patients
- ii. Treatment of choice for young patients with hyperthyroidism
- iii. Propylthiouracil is used for thyrotoxicosis during pregnancy
- iv. Small goitre with thyrotoxicosis.
- v. Preparation of patients for thyroidectomy or radioactive iodine therapy

#### Contraindications

- Hypersensitivity
- Carbimazole is to be avoided during pregnancy and lactation

#### Side effects

- Leucopenia
- Agranulocytosis. Patient on carbimazole should have full blood counts every week
- Allergic rash
- Drug fever
- Arthralgias

#### Q. What are treatment modalities available for thyrotoxicosis?

1. **Antithyroid drugs**—already discussed
2. **Radioactive treatment:** The dose of radioactive iodine  $^{131}\text{I}$  is empirical (usually 5-10 mci orally). A second dose may be repeated after 3 months if no improvement.

#### Indications

- Patients more than 40 yrs of age (after completion of family)
- Recurrence following surgery
- Multinodular toxic goitre (treatment of choice)

#### Contraindications

- Pregnancy

- Mothers desirous of having a child.
- Older patients who refuse to undergo surgery.

#### Side effects

- Hypothyroidism
- Congenital malformations in offsprings
- Susceptibility to carcinogenesis may be increased in the thyroids of children.

### 3. Subtotal thyroidectomy

#### Indications

- Large goitre or multinodular goitre with thyrotoxicosis
- Frequent relapse on drug treatment
- Young patients with hypersensitivity to drug therapy
- Poor drug compliance

#### Side effects

- Vocal cord paralysis due to damage to recurrent laryngeal nerve during surgery
- Wound infection
- Haemorrhage
- Hypothyroidism
- Hypoparathyroidism

### Thyroxine Replacement Therapy

#### Preparations

Liothyronine, thyroxine (L-thyroxine), Liotrix ( $\text{T}_4/\text{T}_3$  4:1)  
Thyroid extract USP.

#### Action

They increase the metabolic rate with subsequent increase in catabolism.

#### Uses

- Hypothyroidism (myxoedema, cretinism), subclinical hypothyroidism, postpartum thyroiditis
- Various conditions associated with subnormal metabolism
- To suppress TSH in simple puberty goitre to reduce its size
- Myxoedematous coma

**Box 3.19:** Dosage and side effects of various thyroid preparations

Preparation	Average daily dose	Side effects
L-thyroxine	100-150 mg/day as single dose (max 300 mg)	Palpitation, tachycardia anginal pain, weight loss, diarrhoea,
L-thyronine	50 mg	restlessness, irritability,
Liotrix (T <sub>4</sub> /T <sub>3</sub> =4:1)	24 units	flushing, headache, sweating
Thyroid extract USP	120-180 mg	

### Precautions

1. In neonatal, infantile and juvenile hypothyroidism, full replacement therapy or large dose therapy should be instituted as soon as possible, otherwise, the chances of normal intellect development and growth will be poor.
2. In patients of myxoedema with heart disease, a small initial dose should be started, otherwise, angina will be precipitated.
3. In some adults, hypothyroidism should be treated rapidly such as myxoedema coma or patients prepared for emergency surgery. In these patients, intravenous administration of L-thyroxine, in conjunction with use of hydrocortisone is indicated, but injectable preparation of thyroid hormone is not available, hence, oral therapy is usually employed.
4. In known or strongly suspected cases of pituitary or hypothalamic hypothyroidism, thyroid replacement should not be instituted until treatment with hydrocortisone has been initiated, since acute adrenal insufficiency will get precipitated by increase in metabolic rate induced by thyroxine.
5. Otherwise, in known case of adult hypothyroidism, start with small dose and then increase the dose at interval of 2 weeks till normal metabolic state is achieved.
6. The parameter of metabolic control is return of TSH to normal or near normal level in hypothyroidism due to thyroid origin; while level of T<sub>3</sub> is parameter of control in supratyroidal hypothyroidism where levels of TSH are erratic and not reliable.

*Doses and side effects (Box 3.19).*

### SOMATOSTATIN (INHIBITOR OF GROWTH HORMONE RELEASE)

#### Actions

It is produced by the pancreas, inhibits the release of GH from pituitary. In addition, it has ability to inhibit secretions of various endocrine and exocrine glands e.g. gastric, pancreatic.

#### Uses

1. In the management of GI haemorrhage from oesophageal varices, gastric or duodenal ulcers or acute erosive or haemorrhagic gastritis.
2. Adjuvant treatment in pancreatic, biliary and intestinal fistulae.
3. Prophylaxis and treatment of post-operative complications following pancreatic surgery.
4. Adjuvant treatment in diabetic ketoacidosis.

*Dose:* 250 mcg by slow I.V bolus over 3-5 min, continuous infusion 3 mg administered over 12 hours by infusion in either saline or 5% dextrose.

*Contraindication:* Pregnancy, immediate postpartum period, lactation

*Side-effects:* Nausea, vomiting, vertigo, flushing

*Precaution:* Type I diabetes in whom blood glucose to be monitored every 3-4 hourly.

### Somatostatin Analogue (Octerotide)

#### Action

It lowers GH level in acromegaly.

### Indications

1. Octreotide is used for short-term treatment of acromegaly prior to pituitary surgery. It lowers GH level to <5 mg/L in 50% cases of acromegaly.
2. Long-term treatment for acromegaly when surgery, dopamine agonists or radiotherapy are ineffective or inappropriate.
3. As an interim measure before radiotherapy becomes effective in acromegaly.
4. It is used in management of GI haemorrhage.

### Dose

Adult Initially 0.05-0.1 mg 2-3 times daily by SC injection. Optimum dose 0.2-0.3 mg/day and maximum 1.5 mg/day.

*Contraindications:* Pregnancy, lactation

*Side effect:* Reaction at injection site, GI upset, gallstones and biliary colic.

Rarely, hyper or hypoglycaemia, loss of hair, hepatic dysfunction, acute pancreatitis

## SOMATOTROPHIN (GH)

### Uses

1. Growth failure in children due to deficiency of endogenous GH.  
Dose: 0.09 IU/kg body weight SC injection daily or 0.02 IU/kg three times a week by SC or IM injection
2. Turner Syndrome (0.09 to 0.1 IU/kg daily by SC injection increasing to 0.11-0.14 IU/kg daily if required)
3. Growth failure in prepubertal children due to chronic renal failure  
Dose: 0.15 IU/kg daily by SC injection

*Contraindication:* Epiphyseal fusion, progressive intracranial lesion

*Side effects:* Hypothyroidism, oedema, pain at injection site and lipoatrophy

## ORAL CONTRACEPTIVES

### Definition

These are the drugs (pills) used against contraception and contain an oestrogen and a progesterone.

### Contraindications

1. Thrombophlebitis or thromboembolic disorders or past history of such disorders.
2. Cerebrovascular or coronary artery disease.
3. Known or suspected carcinoma breast and known or suspected oestrogen dependent neoplasia.
4. Undiagnosed abnormal vaginal bleeding.
5. Known or suspected carcinoma of genital organs.
6. Known or suspected pregnancy.
7. Hepatic dysfunction, cholestatic jaundice or benign intrahepatic cholestasis, Dubin-Johnson or Rotar syndromes.
8. Sick cell anemia
9. Abnormal lipid metabolism
10. Depression, migraine, epilepsy, otosclerosis, inappropriate hyperprolactinaemia, pills to be used with caution in these disorders.

### Adverse effects/caution

1. Use of oral contraceptive may be associated with increased risk of thromboembolism, stroke, myocardial infarction, hepatic adenoma, gall-bladder disease and hypertension. Should any of these occur or be suspected, treatment should be discontinued. The risk of myocardial infarction is increased in females above the age of 40 years especially in the presence of other coronary risk factors.
2. Optic neuritis and retinal vein thrombosis have been reported. Discontinue drug pending examination if there is unexplained sudden partial or complete visual loss.
3. Ectopic as well as intrauterine pregnancy may occur in contraceptive failure.
4. The first spontaneous ovulation after stopping the oral contraceptive is sometime delayed or there is evidence of temporary impairment of fertility in women who discontinue oral contraceptives, but is not a proven fact.
5. Oral contraceptives may diminish the quantity and quality of the milk of lactating women.
6. Chances of benign breast tumours among the user have been well documented.

7. They impair glucose tolerance and predispose to diabetes. In diabetes, they may increase insulin requirement.
8. Oral contraceptive may cause some degree of fluid retention. Certain disorders such as cardiac or hepatic insufficiency, migraine and asthma may be aggravated.
9. Patient should be warned that vulvovaginal moniliasis may occur or recur, and may require appropriate treatment.
10. Pyridoxine and plasma folate levels may be depressed by oral contraceptives, hence, should be supplemented.

### Drug Interactions

1. Antiepileptics (e.g. phenytoin, carbamazepine, ethosuximide), rifampicin, antibiotics (ampicillin, tetracyclines, chloramphenicol), barbiturates, chloral hydrate may reduce the efficacy of oral contraceptives and may lead to contraceptive failure.
2. Oral contraceptives reduce the efficacy of oral anticoagulants.
3. Oral contraceptives reduce the metabolism of antidepressants (imipramine) and lead to increased plasma levels

### Missed Pill

Most of oral contraceptive pills are usually taken on 5th day of menstrual cycle and continued daily for 21 days without break for successful contraception. It must be remembered that the critical time for loss of protection is when a pill is omitted either at the beginning or at the end of a cycle which lengthens the pill free interval (normal interval is 7 days approx). If a woman forgets to take the pill, she should be advised to take it as soon as possible preferably within 12 hours; and if she takes after that period, it may not work. Even when she restarts taking the pill, she may not be protected for next 7 days, hence, alternative family planning method must be adopted for protection.

**Emergency contraception:** It is designed to prevent pregnancy after unprotected sex. The precise mode of action is uncertain but the pill probably works by delaying or inhibiting the ovulation.

*Preparation:* The emergency contraceptive pill consists of 100 mcg of ethinylloestradiol and 0.5 mg of levonorgestrel.

*Dose:* The first dose is to be taken within 72 hours of unprotected sex followed by next dose of same pill 12 hours later. Therefore, 2 tablets will make one course.

*Side effects:* Nausea, vomiting are common side effects and if they occur within 2 hours of ingestion of either the first or second dose, an extra dose should be taken immediately. An antiemetic drug taken one hour before the dose reduces the risk of nausea and vomiting.

*Note:* Only preparation of progesterone can also be used in place of a combined pill. The dose is 750 mcg of levonorgestrel. The dose schedule is exactly the same as described above

*Follow-up:* Abstinence from intercourse or careful use of barrier method should be taken during that cycle. The woman must be seen again after about 3 weeks after treatment to ensure that it has been successful.

### Androgens and Antiandrogens

*Male Sex Hormone (Androgens-testosterone)*

*Action:* In normal male, they inhibit pituitary gonadotrophin secretion and depress spermatogenesis

*Uses*

1. As replacement therapy in castrated males
2. Male hypergonadotrophic hypogonadism (established)
3. Cryptorchidism
4. Delayed puberty (androgen insufficiency)
5. Osteoporosis due to androgen deficiency-androgens act as anabolic hormones
6. Aplastic anaemia. Androgens stimulate haematopoiesis
7. They are used sometimes in cases of advanced breast carcinoma in women

*Contraindications:* Known or suspected male carcinoma breast or prostatic carcinoma; nephrosis, hypercalcaemia, IHD and CHF.

*Caution:* Used with caution in patients of myocardial infarction, renal insufficiency, hypertension, prepubertal boys, nephrotic syndrome.



*Side effects:* Priapism, oligospermia and fluid retention, weight gain, increased bone growth, hypercalcaemia, virilism in women, premature closure of epiphyses, decreased male fertility.

*Dose:* Free testosterone or testosterone propionate

- 25-50 mg I.M twice a week for 4-6 weeks
- Oral testosterone undecanoate: 120-160 mg/day for 2-3 weeks then 40-120 mg daily according to response.

### **Danazol**

It is a synthetic steroid which suppresses pituitary gonadotrophin. It has no oestrogenic or progestational activity.

#### *Uses*

1. It is used in endometriosis, menorrhagia, benign breast disorders, premenstrual syndrome. Dose is variable.
2. Gynaecomastia and precocious puberty 100-400 mg daily for 2-3 months orally. Gynaecomastia due to liver disease is a contraindication.

*Contraindications:* Pregnancy, lactation, porphyria, renal and cardiac oedema

*Adverse reaction:* Nausea, vomiting, rashes, dizziness, flushing, muscle spasm, anabolic effect (fluid retention, weight gain), headache, emotional lability, jaundice, benign intracranial hypertension.

## **GONADOTROPHINS (FSH AND LH)**

#### *Actions*

##### *FSH*

- a. Female: It stimulates maturation of ovarian follicles. It does not cause ovulation
- b. Men: It induces spermatogenesis by acting on seminiferous tubules in the testes

##### *LH*

- a. Female: It acts on the matured follicle causing secretion of oestrogens, follicle rupture, formation of corpus luteum and secretion of progesterone
- b. Male: It stimulates interstitial cells to form androgens.

#### *Preparations*

1. Human chorionic gonadotrophin (HCG) from the urine of pregnant women has activity similar to LH.

2. Gonadotrophin prepared from the urine of pregnant mares has mixed FSH and LH activity but predominantly FSH activity.

#### *Uses*

Combination of FSH and LH are used in:

- i. Anovulatory infertility, threatened habitual abortions
- ii. Hypogonadotrophic hypogonadism in males
- iii. Cryptorchidism
- iv. Oligospermia

*Side effects:* Oedema, headache, mood changes, tiredness, hypersensitivity reactions, sexual precocity

## **Drugs and Impotence**

Impotence simply refers to failure to achieve erection, ejaculation or both.

### **Drug Therapy**

1. *Sildenafil:* It is 5-phosphodiesterase inhibitor, prevents breakdown of GMP(cyclic) in corpora and prolongs smooth muscle relaxation. It is useful in psychogenic impotence. It is taken orally 50-100 mg one hour before intercourse. Side-effects include, headache, nasal congestion, flushing, visual disturbance. It should be avoided in patients with IHD, CVA, sickle cell disease, hypotension and severe hepatic insufficiency.
2. *Alprostadil (Prostaglandin E-1)* Self injection into corpora cavernosa produces erection in men in 90% patients with psychogenic, neurogenic, and mild to moderate vascular impotence. It is also used for neonatal congenital heart defects.

*Contraindications:* The diseases which predispose to prolonged erection e.g. anaemia, leukaemia, multiple myeloma or drugs.

*Dose:* 2-5 mcg by direct intracavernosal injection, increasing by 2.5 mcg to obtain desirable effect e.g. erection for not more than 1 hr. Usual dose is 10-20 mcg and maximum is 60 mcg.

*Side effects:* Painful erection, prolonged erection, haematoma at site of injection, fibrosis, penile deviations, systemic effects (hypotension, arrhythmias, dizziness, headache, vagal shock and collapse).

3. *Penile prosthesis*: They are alternative to impotent patients refractory to other forms of therapy.

### Anabolic Steroids

They include:

- Nandrolone decanoate
- Nandrolone phenylpropionate
- Oxymethalone
- Stanazolol

#### Actions

Anabolic drugs favour the increased retention of nitrogen, calcium, sodium, potassium, chloride and phosphate (positive balance), lead to an increase in skeletal weight, water retention and increased growth of bone (anabolism), oxymethalone in this group has an erythropoietic effect.

#### Uses

1. General debility or wasting diseases
2. Uraemia
3. Senile and post-menopausal osteoporosis
4. Post-surgical convalescence
5. To promote growth in undernourished children
6. Adjuvant to steroid therapy
7. Oxymethalone and stanazolol may be used to stimulate erythropoiesis in aplastic anaemia.

#### Abuse

They are abused for improving performance by athletes.

#### Contraindications

- Pregnancy
- Prostatic and male breast carcinoma
- Selected cases of female breast carcinoma

*Side effects* (Table 3.34).

### RECOMBINANT HUMAN ERYTHROPOIETIN

*Action*: It stimulates the erythropoiesis by its action on the mesenchymal stem cells in the bone marrow. This action is similar to endogenous erythropoietin secreted by the kidneys.

*Indications*: Administration of recombinant erythropoietin is the treatment of choice for anaemia in patients with chronic renal failure both before and after dialysis. Treatment is instituted if the haematocrit is less than 30%.

*Dose*: The starting dose is approximately 25-50 units / kg/ three times a week either subcutaneously (SC) or intravenously (IV). Increase in dosage may be needed after 8-12 weeks with monitoring of haematocrit after every 2-4 weeks.

#### Causes of Erythropoietin Resistance

- Iron deficiency
- Aluminium toxicity

**Table 3.34:** Common anabolic steroid

Drug	Dosage	Side effects	Comment
• Nandrolone phenylpropionate	Adult 25-50 mg I.M/week Children 5-10 mg I.M/week	• Oedema, virilisation in women, hypercalcaemia	• Short-acting preparation
• Nandrolone decanoate	Adult: 25-50 I.M every 3 weeks Children: 5-15 mg I.M after every 3 week Oral: Adult. 2 mg tid Children. 2 mg bid	- same -	• Long-acting preparation
• Stanazolol	Oral: 2-4 mg tid with meals	• Hepatotoxicity, virilisation in women and pre-pubertal children, rashes, dyspepsia, cramps, headache.	• Can be used in aplastic anaemia
• Oxymethalone	Oral: 2 mg/kg/day in divided doses	• Hepatotoxicity, jaundice, oedema, virilisation, hypercalcaemia, hyperlipidaemia	• For aplastic anaemia, therapy is used for 2-6 months

- Marrow fibrosis from hyperparathyroidism
- Chronic inflammatory states
- Primary hematological disease.

*Special precaution:* About 30% patients on chronic erythropoietin therapy may have increase in severity of hypertension which should be treated appropriately by antihypertensive therapy.

*Causes of anaemia in CRF:* The anaemia is normocytic normochronic. It is due to;

- Iron or folate or both deficiency
- Haemolysis (extracorporeal destruction)
- Bone marrow suppression by uraemic toxins
- Impaired erythropoietin synthesis
- Bleeding from GI tract (chronic blood loss)
- Blood loss is exaggerated in patients on haemodialysis because of use of heparin during dialysis and the retention of blood in the dialyzer and associated tubing.

## CORTICOSTEROIDS

The adrenal cortex secretes glucocorticoid (hydrocortisone or cortisol) which has major effect on intermediary metabolism, and mineralocorticoid (aldosterone) which has major effect on minerals (sodium and potassium) metabolism.

Normal glucocorticoid secretion is 15-30 mg with pronounced circadian rhythm; increases upto 300 mg during acute stress.

Normal mineralocorticoid secretion is 50-250 mg. Corticosteroids secretion is controlled by ACTH by feedback mechanism.

### Actions

1. **Metabolic functions:** Physiological effects of glucocorticoids include the regulation of carbohydrate, protein, nucleic acid and lipid metabolism.
  - *Carbohydrate metabolism:* Glucocorticoids raise blood sugar levels by promoting hepatic glucose synthesis (gluconeogenesis) and inhibit peripheral utilisation of glucose by inhibiting insulin action (anti-insulin effect)

- *Protein metabolism:* Glucocorticoids result in protein catabolism with the result that there is increased protein breakdown and nitrogen excretion. This action results in mobilisation of proteins from peripheral tissues such as bone, muscle, skin and connective tissue for catabolism
  - *Nucleic acid:* They inhibit the synthesis of nucleic acid in most body tissues
  - *Fat metabolism:* They regulate fatty acid mobilisation by enhancing the activation of cellular lipase by lipid-mobilising hormones (e.g. catecholamines and pituitary peptides). This results in redistribution of fat
2. **Anti-inflammatory:** They have anti-inflammatory properties probably related to suppression of inflammatory cytokines (inhibit the production and action of the mediators of inflammation e.g. lymphokines and prostaglandins).
  3. **Antiallergic:** They inhibit the release of allergic substances from the eosinophils.
  4. **Immunosuppressive:** At higher doses (1 mg/kg), the antibody production is reduced and lysosomal membranes are stabilised. Due to this effect, corticosteroids are used as immunosuppressive drugs.
  5. **Water and electrolyte metabolism:** Cortisol at high doses promotes renal tubular sodium reabsorption and its subsequent retention and in exchange causes loss of potassium in the urine. There is passive movement of water along with sodium. This results in hypokalaemia with fluid and Na<sup>+</sup> retention resulting in hypertension and oedema.
 

It also regulates the extracellular fluid volume by retarding the migration of water into the cells. This fluid overload is overcome by solute free water clearance by inhibition of vasopressin secretion by corticosteroids. This action prevents water intoxication.
  6. **Suppression of pituitary peptides (ACTH,  $\beta$ -endorphin and  $\beta$ -lipoproteins):** Cortisol suppresses the secretion of pituitary peptides and the secretion of hypothalamic CRH and vasopressin. The suppression of ACTH and CRH is via pituitary adrenal axis. Due to this action, it is used as a diagnostic tool

(dexamethasone suppression test) for diagnosis and differential diagnosis of Cushing's syndrome.

### Uses

Because of above mentioned actions, they are systemically used in variety of disorders. Before using them, one must consider that "*they are like a glass to be handled with care*". Therefore, corticosteroids should not be used unless the benefits clearly outweigh the hazards. In any event the lowest dose which will produce desired response should be employed. In certain diseases such as exfoliative dermatitis, pemphigus, acute leukaemia, higher doses may be required justifiably because complications of treatment are likely to be less serious than the effects of the disease itself. The initial dose of the drug should be tapered slowly so as to avoid "Addisonian crisis". Their prolonged use may result in "steroid-dependence". The common uses are given in the Table 3.35.

### Side Effects

The clinical picture of Cushing's syndrome is due to excessive secretion of endogenous glucocorticoids. If corticosteroids are given from outside for prolonged period, will also result in features simulating Cushing's syndrome (Cushingoid features), conveniently called *iatrogenic Cushing's syndrome*. The side effects are summarized in the Table 3.36.

### Q. What are life-saving indications of steroids?

1. **Adrenal crisis:** It is acute adrenal insufficiency precipitated by sepsis, trauma, anticoagulant therapy or sudden withdrawal of steroids from a patient with presumed adrenal atrophy owing to chronic steroid administration.
2. **Acute systemic anaphylaxis.**
3. **Acute severe asthma** with hypoxia (status asthmaticus).
4. **Acute cerebral oedema.**
5. **Waterhouse-Friderichsen syndrome:** It is acute adrenal insufficiency associated with septicaemia due to *Pseudomonas* or meningococemia in children without an evidence of prior adrenal insufficiency (healthy children).

**Table 3.35:** Common indications for systemic corticosteroids

1. <b>GI tract disorders</b>
• Coeliac disease (gluten-induced enteropathy)
• Inflammatory bowel disease
2. <b>Liver disease</b>
• Autoimmune hepatitis
• Alcoholic liver disease (severe)
• Primary biliary cirrhosis
3a. <b>Lymphoreticular disorders</b>
• Hodgkin's disease (MOPP regimen)
• Non-Hodgkin lymphoma (CHOP regimen)
3b. <b>Skin disorders</b>
• Exfoliative dermatitis
• Skin allergies
• Pemphigus
• Anaphylaxis (systemic) and urticaria
4. <b>Blood disorders</b>
• Autoimmune haemolytic anaemia
• Acute leukaemias
• Multiple myeloma (melphalan plus prednisolone)
• Idiopathic thrombocytopenic purpura
• Blood transfusion reactions
5. <b>Joint and connective tissue disorders</b>
• Rheumatoid arthritis
• Collagen vascular disorders such as SLE, dermatomyositis, Sjögren's syndrome
• Eosinophilic fasciitis
• Relapsing polychondritis
• Systemic vasculitis
6. <b>Neurological disorders</b>
• Cerebral oedema
• Demyelinating disorders
• Bell's palsy
• Myasthenia gravis
7. <b>Respiratory disorders</b>
• Bronchial asthma
• Hypersensitivity pneumonitis (severe)
• Idiopathic pulmonary fibrosis (interstitial lung disease)
• ARDS (early stage)
8. <b>Renal disorders</b>
• Immune-complex glomerulonephritis and nephrotic syndrome
• Nephropathy associated with collagen vascular disorders
• Hypersensitivity nephropathy
9. <b>Cardiovascular disorders</b>
• Acute rheumatic carditis in children
• Some cases of myocarditis associated with conduction blocks
10. <b>Endocrinal disorders</b>
• Adrenocortical insufficiency (Addison's disease) or following bilateral adrenalectomy
• Panhypopituitarism
• Thyrotoxic crisis
• Grave's ophthalmopathy (severe)
• Subacute thyroiditis

**Table 3.36:** Side effects of systemic corticosteroids

<b>Endocrine</b>	<b>Musculoskeletal</b>
<ul style="list-style-type: none"> <li>• Moon-like face</li> <li>• Truncal obesity, camel hump</li> <li>• Excessive hair growth (hirsutism)</li> <li>• Impotence</li> </ul>	<ul style="list-style-type: none"> <li>• Myopathy and weakness</li> <li>• Osteoporosis, spontaneous fractures</li> <li>• Avascular necrosis</li> <li>• Suppression of bone growth in children</li> </ul>
<ul style="list-style-type: none"> <li>• Menstrual irregularity</li> <li>• Growth suppression</li> <li>• Suppression of hypothalamo-pituitary-adrenal axis</li> </ul>	<b>GI tract</b>
<b>Metabolic</b>	<ul style="list-style-type: none"> <li>• Peptic ulcer</li> <li>• Pancreatitis</li> </ul>
<ul style="list-style-type: none"> <li>• Fluid and sodium retention leading to oedema</li> <li>• Negative <math>\text{Ca}^{++}</math>, <math>\text{K}^+</math> and nitrogen balance</li> <li>• Hyperglycaemia</li> <li>• Hyperlipoproteinaemia</li> <li>• Hypokalaemic alkalosis</li> </ul>	<b>Cardiovascular</b>
<b>Skin</b>	<ul style="list-style-type: none"> <li>• Hypertension</li> <li>• CHF</li> </ul>
<ul style="list-style-type: none"> <li>• Acne, striae (pink)</li> <li>• Bruising</li> <li>• Skin atrophy</li> <li>• Impaired wound healing</li> </ul>	<b>Ocular</b>
<b>Immunological</b>	<ul style="list-style-type: none"> <li>• Glaucoma</li> <li>• Cataract</li> </ul>
<ul style="list-style-type: none"> <li>• Reactivation of tuberculosis</li> <li>• Suppression of delayed hypersensitivity (tuberculin test will be negative in a person on steroids)</li> <li>• Susceptibility to infections</li> </ul>	<b>CNS</b>
	<ul style="list-style-type: none"> <li>• Change in mood and personality</li> <li>• Steroid psychosis</li> <li>• Benign intracranial hypertension</li> </ul>

6. *Acute attack of multiple sclerosis or acute disseminated encephalomyelitis.*

7. *Unexplained shock.*

#### Contraindications

The patients must be screened for following disorders before use either by history or by investigations.

1. *Chronic infection* such as tuberculosis. Steroids may reactivate the tuberculosis. It should not be used in presence of viral and fungal infections. In addition, person on steroids should not undergo immunisation.
2. *Diabetes mellitus*. Steroids may unmask or aggravate diabetes mellitus. Patient of glucose intolerance may develop frank diabetes called *chemical diabetes*.
3. *Osteoporosis* due to any cause.
4. *Peptic ulcer, gastric hypersecretion or esophagitis*. There will be exacerbation of symptoms and increased risk of peptic ulcer perforation.
5. Hypertension, CHF, thromboembolic tendencies.
6. Psychological diseases—psychosis
7. Renal failure.

#### Preparations

The various preparations with their duration of action and glucocorticoid and mineralocorticoid activity are summarized in the Table 3.37.

**Table 3.37:** Commonly used glucocorticoid preparations

Name	Biological half life (hrs)	Dose	Comment
<b>Short acting</b>	< 12 hours	I.V 100-200 mg after 6 hrs	<ul style="list-style-type: none"> <li>• They have equal glucocorticoid and mineralocorticoid activity</li> </ul>
Hydrocortisone			
Cortisone			
<b>Intermediate acting</b>	12-36 hrs		<ul style="list-style-type: none"> <li>• They are 4-5 times more potent than short acting drugs</li> </ul>
Prednisone		Oral 10-20 mg/day as single dose	<ul style="list-style-type: none"> <li>• They have potent glucocorticoid activity with less mineralocorticoid effect</li> </ul>
Prednisolone		60 mg/day (severe case)	
Methyl prednisolone		IV or IM 1gm/day	<ul style="list-style-type: none"> <li>• Methyl prednisolone has least mineralocorticoid effect</li> </ul>
Triamcinolone			
<b>Long-acting</b>	> 48 hrs		
• Betamethasone		Oral 0.5-5 mg/day I.V or I.M 4-20 mg three or 4 times a day if required	<ul style="list-style-type: none"> <li>• They are 5 times more potent than intermediate acting and 20-25 times than short acting drugs</li> </ul>
• Dexamethasone		Oral 0.5-10 mg IV or IM 0.5-20 mg repeated as required	<ul style="list-style-type: none"> <li>• They have excellent glucocorticoid activity with least mineralocorticoid effect</li> </ul>



*Precautions before use*

- Use them when absolutely necessary. Balance the risks vs benefits of steroids
- Use the smallest effective dose. The dosage of steroids is less when used as anti-inflammatory agents than for immunosuppression
- Withdrawal of glucocorticoids following long-term use: Reduce the dose of steroid gradually by 5 mg every 3-5 days and eventually to discontinue a daily steroid dose under most circumstances. Withdrawal of steroids should be initiated by first shifting the patient on alternate day schedule on the same dose. Patients who have been on alternate day programme for a month or more experience less difficulty during termination regimen. The dose is gradually reduced and finally discontinued after a replacement dose has been reached (e.g. 5 to 10 mg prednisolone)

In patients on high dose daily steroid therapy, it is advised to reduce the dose slowly to 20 mg prednisolone daily as a single dose before shifting to alternate-day therapy. If a patient cannot tolerate an alternate-day regimen, consideration should be given to the possibility that the patient has developed primary adrenal insufficiency.

- When used as replacement therapy for Addison's disease, two-third dose should be given in the morning and one-third dose in the evening to maintain circadian rhythm.
- For long-term use of steroids, initial steroid program often requires daily or more frequent doses of intermediate acting steroid (prednisolone) to achieve the desired effect. Once desired effect is achieved, attempt should be made to switch on alternate-day-morning programme before withdrawal.

*Route of administration*

The routes are oral, parenteral, intra-ocular, intradermal, topical, intrarectal (retention enema) intrapleural and intrarticular.

**ACTH**

- It is a naturally synthesised hormone by pituitary gland

*Uses*

- It is used in pituitary adrenal insufficiency
- It is used as a diagnostic test for differential diagnosis of Cushing's syndrome to determine its cause
- It can be used in all other conditions where steroids are indicated except as replacement therapy where steroids only are given.

**Q. What are indications for high-dose corticosteroid therapy?**

- Status asthmaticus (acute severe asthma)
- Cerebral oedema
- For immunosuppression
- Unexplained shock
- Enteric encephalopathy: It is used as an adjunct to antimicrobial therapy.

**INFECTIONS, INFESTATIONS AND VACCINATION****ANTIMICROBIAL DRUGS/AGENTS**

- These are drugs/agents used against microbes
- Infection means presence of bacteria in the host
- Disease means reaction to the infection

*Stages of Bacterial Infection and Disease*

- I. Bacterial entry and colonization of the host
- II. Invasion by bacteria and growth in host tissue and liberation of toxic substances (toxins)
- III. The host response.

The organisms causing infection are given in the Box 3.20.

**Box 3.20: Gram-positive and negative organisms****Gram-positive organisms**

- *Cocci* e.g. staphylococci, streptococci
- *Bacilli* e.g. *C. diphtheria*, *listeria*, *clostridium*, *B. anthrax*

**Gram-negative organisms**

- *Cocci* e.g. meningococci, gonococci
- *Bacilli* e.g. *brucella*, *bordetella* (pertussis), *haemophilus*, *V. cholerae*, *enterobacteriaceae* (e.g. *E. coli*, *salmonella*, *shigella*), *compylobacter*, *helicobacter*, *yersinia*, *tularemia*, *pseudomonas*, *klebsiella*, *legionella* etc.

### Mechanisms of Action

1. *Inhibition of cell wall synthesis*
  - $\beta$ -lactams (penicillins and cephalosporins)
  - Vancomycin
  - Bacitracin
2. *Inhibition of protein synthesis*
  - Macrolides
  - Lincosamides
  - Chloramphenicol
  - Tetracyclines
  - Aminoglycosides
  - Mupirocin
3. *Inhibition of bacterial metabolism*
  - Sulphonamides and trimethoprim
4. *Inhibition of nucleic acid synthesis or activity*
  - Rifampicin
  - Metronidazole
  - Nitrofurantoin
  - Quinolones
  - Novobiocin
5. *Alteration of cell membrane permeability*
  - Gramicidin
  - Polymyxins

### Q. What is spectrum and uses of penicillin G?

**Ans.** The organisms sensitive to penicillin and diseases caused by them are as follows;

Organisms	Diseases
<ul style="list-style-type: none"> <li>• Spirocheates</li> <li>• Streptococci (group A and B viridan and streptococcus pneumoniae)</li> </ul>	Syphilis, yaws, leptospirosis Group A and B streptococcal infections i.e. upper and lower respiratory tract infections, urinary tract infection, cellulitis, endocarditis, peridental infection, brain abscess, meningitis, puerperal sepsis, empyema
<ul style="list-style-type: none"> <li>• Meningococcal infection</li> <li>• Neisseria</li> </ul>	Meningococemia and meningococcal meningitis Gonococcal infections i.e. urethritis
<ul style="list-style-type: none"> <li>• Clostridia except myonecrosis</li> </ul>	Tetanus and clostridial infection, e.g. clostridia perfringes (gas gangrene). Penicillin is not effective against C. difficile infection i.e. pseudomembranous colitis
<ul style="list-style-type: none"> <li>• Actinomyces</li> <li>• Bacteriodes</li> <li>• Anthrax</li> </ul>	Actinomycosis Peri-dental infections Anthrax infection

### Indications of Ampicillin/Amoxycillin

- i. In addition to above mentioned diseases where ampicillin can be used, the other indications are infections caused by;
  - *E. coli* producing urinary tract infection
  - Salmonella causing enteric fever and salmonella enteric infections
  - Shigella causing bacillary dysentery
  - *H. influenzae* causing meningitis
- ii. Ampicillin/amoxycillin is used in regimen for *H. pylori* eradication.

### Name the $\beta$ -lactamase inhibitors and What are their Uses?

$\beta$ -lactamase inhibitors are;

- Clavulanic acid
- Sulbactam
- Tazobactam

### Uses

They are added to ampicillin, amoxycillin, ticarcillin or piperacillin to extend the spectrum of these agents to cover many other organisms such as *E. coli*, *Klebsiella*, *B-proteus*, *H. influenzae* and  $\beta$ -lactamase producing staphylococci.

### Q. Name the antipseudomonal penicillins

- Read the classification (Table 3.38).

### Q. Name the long-acting penicillins. What are its indications?

A. Benzathine penicillin—(commercial vials contain, 6 millions and 12 millions units for IM use)

### Oral penicillins

- Becampicillin hydrochloride
- Phenoxymethyl penicillin (penicillin V)
- Penicillin potassium

### Uses

- Prophylaxis against SABC

**Table 3.38:** Classification and parenteral preparations of  $\beta$ -lactam antibiotics

Class	Parenteral preparations
1. <b>Penicillins</b>	
A. <i><math>\beta</math>-lactam susceptible</i>	
• Narrow spectrum	Penicillin G, procaine penicillin, benzathine penicillin
• Enteric active	Ampicillin, amoxicillin
• Enteric-active and anti-pseudomonal	Carbenicillin, ticarcillin mezlocillin, azlocillin, piperacillin
B. <i><math>\beta</math>-lactam-resistant</i>	
• Antistaphylococcal	Methicillin, oxacillin, nafcillin
• Combination with $\beta$ -lactamase inhibitors	Ticarcillin plus clavulanic acid Ampicillin plus sulbactam Piperacillin plus tazobactam
2. <b>Cephalosporins</b>	
A. <i>First generation</i>	cefazolin, cephalothin, cephadrine, cephalexin, cefadroxil
B. <i>Second generation</i>	
• Haemophilus active	cefamandole, cefuroxime, cefonicid, ceforanide
• Bacteriodes active	cefoxitin, cefotetan, cefmetazole
C. <i>Third generation</i>	
• Extended spectrum	ceftriaxone, cefotaxime, ceftizoxime
• Extended spectrum and antipseudomonal	ceftazidime, cefoperazone
D. <i>Fourth generation</i>	cefepime, cefpicome
3. <b>Carbapenems</b>	Imipenem cilastatin
4. <b>Monobactams</b>	Aztreonam

- Used for treatment of recurrent streptococcal infections where therapy for prolonged period with penicillin is desired such as syphilis, pyoderma, post-traumatic tetanus

#### Side Effects

It includes

- Skin rashes
- Pruritus
- Urticaria
- Herxheimer's reaction e.g. *Jerisch Herxheimer reactions*
- GI tract symptoms—nausea, vomiting, pseudomembranous colitis
- Blood—thrombocytopenia, leucopenia, eosinophilia
- Rise in transaminases
- Irritation at the injection site. IV therapy may cause vein irritation and phlebitis
- High parenteral therapy may produce CNS toxicity including convulsions

- Prolonged therapy will result in opportunistic infection by resistant organisms

#### Precautions

Serious and sometimes fatal hypersensitivity reactions (anaphylactoid) may occur, hence, care should be taken in patients with known allergies such as hay fever, asthma, urticaria, nasal allergy etc. It should be used with caution in patients with infectious mononucleosis, or lymphatic leukaemia since they are susceptible to penicillin induced rashes. During prolonged therapy, blood counts, hepatic and renal functions are to be monitored.

#### Dosage Schedule

See Table 3.39.

#### Injectable penicillin combinations

The common combinations used are;

- Ampicillin plus cloxacillin
- Ampicillin plus salbactam

Table 3.39: Drugs dose and duration

<b>Meningitis</b>		
1. Pneumococcal	Benzyl penicillin or cefotaxime	24 million units of penicillin/24 hr given in divided doses at 4 hours interval or cefotaxime 2 g every 6 hr. Duration of therapy is 10-14 days.
2. Meningococcal	Penicillin as above	In addition give rifampicin for 2 days before hospital discharge
3. <i>H. influenzae</i>	Chloramphenicol or cefotaxim	Chloramphenicol (1 g I.V every 6 hrly) or cefotaxime IV 2 g after every 6 hrs.
<b>Endocarditis</b>		
	1. Penicillin sensitive streptococci	
<i>Penicillins injectable preparations sharing pharmacological class</i>		
Generic name and their combinations		
<i>Ampicillin (injections and oral)</i>	<i>Amoxycillin (available as oral and parenteral prep)</i>	
<i>Combinations</i>	<i>Combinations</i>	
• Ampicillin plus cloxacillin	Amoxicillin + cloxacillin	
• Ampicillin + cloxacillin	Amoxicillin + clavulanic acid	
• Ampicillin + sulbactam		
• Ticarcillin + clavulanic acid	Piperacillin Tazobactam	

- Amoxycillin plus cloxacillin
- Amoxycillin plus clavulanic acid
- Ticarcillin plus clavulanic acid

#### *Monotherapy vs Combination Therapy*

The common rule for antibacterial therapy is that if the infecting organism is identified, the most specific agent according to culture and sensitivity may be used. The advantage of monotherapy are;

- It does not alter the normal flora and thus limits the overgrowth of resistant nosocomial organisms e.g. *candida albicans*, enterococci, *clostridium difficile* or methicillin resistant staphylococci.
- It is devoid of potential toxicity of multi-drug regimens.
- Less costly.

#### *Advantage of Combination Therapy*

In certain circumstances, there is need for the use of more than one antimicrobial agent such as;

- Prevention of emergence of resistant mutants

- Synergistic or additive activity. The combination therapy may be more effective if it contains drugs having synergistic action. The best example is combination of trimethoprim plus sulphamethoxazole (cotrimoxazole)
- Infections caused by multiple potential pathogens e.g. intra-abdominal or pelvic abscess, brain abscess, infection of a limb in diabetics, fever in neutropenic patients, aspiration pneumonia in hospitalised patients, septic shock or sepsis syndrome.

#### *Action of penicillins*

All penicillins exert a bactericidal action against susceptible bacteria by inhibiting cell wall synthesis.

#### *Spectrum of penicillins*

- Narrow spectrum penicillins:** Benzathine penicillin, benzyl penicillin, phenoxymethyl penicillin and procaine penicillin have narrow spectrum of activity and are mainly active against gram-positive bacilli, both gram-positive and gram-negative cocci and spirochaetes.

Cloxacillin and flucloxacillin have a similar spectrum of activity to benzylpenicillin but are also active against penicillinase ( $\alpha$  lactamase) producing organism such as *S. aureus*.

2. **Broad spectrum penicillins:** Amoxycillin, ampicillin, carbenicillin have a broader spectrum of activity than benzylpenicillin because of being active against a much larger number of gram-negative organisms including *E. coli*, *Salmonella* and *H. influenzae*. Carbenicillin is also active against *Pseudomonas aeruginosa*.

## Cephalosporins

### Action

The cephalosporins are broad-spectrum bactericidal agents which inhibit bacterial cell wall synthesis.

### Spectrum

Susceptible organisms include a wide variety of gram-positive and gram-negative organisms. These include a *haemolytic streptococci*, *strept. pneumoniae*, *staph. aureus* (both penicillin sensitive and resistant), *Neisseria gonorrhoea*, *N. meningitidis*, *P. mirabilis* and some strains of *E. coli*, *Klebsiella sp.* and *H. influenzae*.

Second and third generations cephalosporins show improved activity against a range of organisms including *E. coli*, *indole-positive Proteus sp.*, *enterobacter* and *haemophilus sp.* Third generation cephalosporins also show activity against *Pseudomonas aeruginosa*.

### Uses

Based on their antibacterial spectrum, they are used in treatment of;

- i. Respiratory tract infections
- ii. Genitourinary infections
- iii. Soft tissue infections
- iv. Bone and joint infections
- v. Septicaemia
- vi. Intra-abdominal infections

### Preparations

Both oral and parenteral preparations are available (Box 3.21).

**Box 3.21: Preparations of cephalosporins**

	Oral	Parenteral
First generation	Cephalexin	—
Second generation	Cefaclor cefadroxil	—
Third generation	—	cefotaxime, cefoperazone, ceftriaxone ceftazidime
Fourth generation	—	Cefepime

### Side Effects

- False positive reactions in the urine for glucose
- Blood e.g. positive direct Coomb's test, leucopenia, eosinophilia, granulocytopenia
- Liver e.g. transient rise in transaminases (SGOT/SGPT), and alkaline phosphatase
- Kidney e.g. elevation in serum creatinine and blood urea especially with first generation
- GI tract e.g. nausea, abdominal pain, diarrhoea, vomiting, phlebitis at injection sites
- Hypersensitivity reactions e.g. fever, rash (maculopapular), urticaria

### Precautions

- Impaired renal function. The third generation are safe. Dose may be adjusted
- Overgrowth of opportunistic infections after prolonged use
- Use first generation cephalosporin with caution in patients receiving aminoglycoside antibiotic as combination may potentiate nephrotoxicity.

## Macrolides

### Drugs/Preparations

*Erythromycin*, *roxithromycin*, *azithromycin*, *clarithromycin*, all are oral preparations. No parenteral preparation is available.



**Actions**

They inhibit bacterial protein synthesis.

**Bacterial Spectrum**

Erythromycin	Azithromycin	Clarithromycin
Streptococci, pneumococci staphylococci, mycoplasma <i>H. influenzae</i> , Legionella, <i>N. gonococci</i> , <i>T. pallidum</i> and Chlamydia	Same as erythromycin but more effective against Chlamydia infection	Same as erythromycin. It is used in combination with proton pump inhibitor for gastric infections due to <i>H. pylori</i>

**Indications**

- Skin infections
- Ear infections
- Respiratory infections. Drug of choice for mycoplasma pneumoniae
- Gonococcal infections
- Used as an alternative to penicillin in patients with penicillin hypersensitivity such as prophylaxis against bacterial endocarditis
- Clarithromycin is used in combination with proton pump inhibitor for gastric infection caused by *H. pylori*.

**Side Effects**

- GI symptoms—nausea, vomiting, abdominal pain
- Skin—rashes, urticaria, allergic reactions such as anaphylaxis
- Cholestatic jaundice

**Aminoglycosides****Actions**

The aminoglycosides are bactericidal agents *in vitro* at low concentrations with activity limited to facultative gram-negative bacteria and staphylococci.

**Bacterial Spectrum**

- Gram-negative bacilli e.g. *E. coli*, *Kleb. pneumoniae*, *Pseudomonas*, *B. proteus*, *Enterobacter*, *Serratia* species.
- *Staphylococci* including penicillin-resistant strains

**Preparations**

Oral—Neomycin

Parenteral—gentamicin, amikacin, tobramycin, kanamycin, streptomycin, spectinomycin

**Indications**

1. They are among the drug of choice for any suspected gram-negative bacterial infection particularly in neutropenic patients and in patients with haematological malignancies.
2. They are synergistically bactericidal in combination with a penicillin, hence, the combination is used for the treatment of staphylococcal, enterococcal or streptococcal viridans endocarditis.
3. They are usually combined with a  $\beta$ -lactam antibiotic for treatment of gram-negative septicaemia.
4. They are used for severe respiratory tract infections.
5. Streptomycin is still one of the drugs of choice in initial therapy for tularemia, plague, glanders and brucellosis. It is first-line agent for the treatment of tuberculosis. Amikacin, kanamycin, capreomycin all injectable preparations are used as second line antitubercular drugs.
6. Neomycin is also used topically for skin infections due to susceptible organisms and orally for sterilisation of gut in hepatic encephalopathy.

**Side Effects**

- Reversible ototoxicity, nephrotoxicity, headache, rashes, thrombocytopenia and joint pain.
- Streptomycin in addition to above produces peri-oral paraesthesias, hepatotoxicity and superinfections.

**Special Precautions**

Being nephrotoxic, renal function should be monitored and dose of the drug (e.g. gentamicin a commonly used aminoglycoside) should be adjusted according to serum creatinine level.

**Contraindications**

- Severe renal failure
- Pregnancy. It crosses the placenta and can cause eighth nerve damage in the foetus

- Neonates (except in life-threatening situations)
- Streptomycin is contraindicated in patients receiving neuromuscular blockers
- Hypersensitivity

### Lincosamides

#### Action

They inhibit bacterial protein synthesis. Bacterial spectrum includes gram-positive cocci similar to erythromycin. It is effective against anaerobes.

#### Preparations

It includes

- Clindamycin (parenteral)
- Lincomycin (oral and parenteral)

#### Uses

- Staphylococcal bone and joint infections
- Peritonitis
- Endocarditis prophylaxis
- Anaerobic infections

#### Contraindications

- Diarrhoeal states
- Neuromuscular blocking agents use

#### Special Precautions

- Hepatic and renal impairment
- Discontinue its use if persistent diarrhoea or colitis develops
- Monitor liver function and blood counts on prolonged therapy
- Avoid it during pregnancy and breast feeding

#### Side Effects

*GI tract*—diarrhoea, pseudomembranous colitis

*Liver*—jaundice, altered liver functions

*Skin*—rash, pain, induration and abscess after IM inj

*Blood*—agranulocytosis and thrombocytopenia.

### Chloramphenicol

#### Action

It inhibits bacterial protein synthesis (bacteriostatic).

#### Microbial Spectrum

- All species of rickettsia
- Large viruses of psittacosis, lymphogranuloma group
- Gram-negative bacterial infections e.g. *Salmonella typhi*, *Haemophilus influenzae*, *B. pertussis*, *E. coli* and *Shigella*, *Brucella*, *Klebsiella* and *Proteus sp.* and *Treponema pallidum*
- It's activity against gram-positive bacteria is much less than penicillin

#### Uses

1. This antibiotic is rarely used in adults because of the rare idiosyncratic side effect of irreversible bone-marrow aplasia. It is used only when it is the only suitable drug in the treatment of life-threatening infections.
2. It remains one of the drug of choice for treatment of *typhoid* and *paratyphoid* fevers, *plague*, *H. influenzae* and other severe *Salmonella* infections.
3. It is still useful for treatment of *brucellosis* and *Pneumococcal meningitis*.

#### Contraindications

- Hypersensitivity
- Porphyria
- Pregnancy and lactation
- Concomitant use of penicillin

#### Precautions

- Avoid repeated use and prolonged treatment
- Monitor regular blood counts before and after therapy
- Reduce the dose during hepatic and renal impairment
- There is possibility of superinfections

#### Drug Interactions

- Rifampicin
- Phenobarbitone and phenytoin

- Anticoagulants (warfarin) and sulphonamides action is enhanced

### Side Effects

- **Blood dyscrasias** e.g. aplastic anaemia (both idiosyncrasy and dose related) and bone marrow suppression
- **Grey syndrome** in new-born and premature infants (Grey-baby)
- **GI symptoms**—nausea, vomiting, diarrhoea, dry mouth
- **CNS**—optic and peripheral neuropathy
- **Skin**—allergic skin reactions
- **Nocturnal haemoglobinuria reported.**

### Preparation

Both oral and injectable (vial)

### Tetracyclines

#### Actions

They have broad spectrum bacteriostatic (inhibit protein synthesis) activity. Their value has considerably decreased owing to increased bacterial resistance.

#### Microbial Spectrum

##### Susceptible organisms include

- Chlamydia infection (trachoma, psittacosis, salpingitis, urethritis and lymphogranuloma venereum). Doxycycline is drug of choice
- Rickettsia (Q fever)
- Mycoplasma (respiratory and genital infections)
- Brucella (doxycycline with rifampicin)
- Spirochaete (Lyme disease and relapsing fever leptospirosis, syphilis) infection
- Actinomycosis (used when there is penicillin hypersensitivity because penicillin is the drug of choice)
- Gram-positive cocci
- Vibrio infection (cholera)

#### Preparations

Tetracycline—only oral

Oxytetracycline (both oral and injectable—tetracycline)

Chlortetracycline (oral)

Dimethylchlortetracycline (oral)

Doxycycline (oral)

Minocycline (oral)

#### Uses

- Acute exacerbation of chronic bronchitis
- Acne vulgaris
- Cholera
- Brucellosis, chlamydia, mycoplasma and rickettsial infections
- Pleural effusions due to malignancy or cirrhosis. It is instilled into pleural effusion for pleurodesis
- Pelvic inflammatory disease in combination with metronidazole

#### Side Effects

- **GI symptoms**—gastric upsets, glossitis, stomatitis, proctitis
- **Skin**—rashes, photosensitivity
- **Superinfection** e.g. by fungi
- **Teeth discolouration** (yellow-grey brown), enamel hypoplasia, reduces fibula growth in children
- **Allergic reactions**, pain and local irritation on IM injection
- **Hepatotoxicity**

#### Contraindications

- Pregnancy
- SLE
- Lactation
- Severe renal insufficiency

#### Special Precaution

- Avoid its use with milk, food, antacid, iron supplement, oral contraceptive, penicillin and anticoagulants
- Avoid its use in children below 8 yrs
- Reduce the dose in renal failure
- Use carefully in hepatic insufficiency.

### Fluoroquinolones

The fluoroquinolones have excellent activity against most facultative gram-negative rods, fair activity against

staphylococci, variable to poor activity against streptococci and no activity against anaerobes.

#### Actions

They are bactericidal drugs and act by inhibiting the enzyme responsible for maintaining the structure of DNA.

#### Preparations

Both oral and parenteral preparations are available. The oral absorption of these drugs is good to excellent and there is greatest activity against *P. aeruginosa* especially of ciprofloxacin.

#### Formulations

##### Parenteral

- Ciprofloxacin
- Ofloxacin
- Pefloxacin

##### Oral

- Norfloxacin
- Ciprofloxacin
- Ofloxacin
- Lomefloxacin
- Levofloxacin
- Pefloxacin
- Sparfloxacin
- Gatifloxacin

#### Indications

1. Oral norfloxacin can be used for urinary tract infections and has been recommended for infectious diarrhoea.
2. However, quinolones other than norfloxacin should be used for gram-negative infections. The injectable ciprofloxacin and ofloxacin are best for this purpose.
3. The quinolones are among the drug of choice for complicated urinary tract infections, bacterial gastroenteritis and typhoid fever and may be useful in therapy for chronic infections caused by gram-negative organisms such as osteomyelitis and chronic otitis externa.
4. They are useful in respiratory and soft tissue infections and gonococcal infections.

5. They are used in prophylaxis in surgery and endoscopy.

6. Ofloxacin and ciprofloxacin are used as second-line antitubercular drugs.

#### Cautions

Fluoroquinolones should be used with caution in patients with epilepsy or a history of epilepsy, in hepatic and renal impairment, in pregnancy, during breast feeding, and in children and adolescents (arthropathy has developed in weight-bearing joints in young animals but human evidence lacking).

#### Side Effects

##### Common

- **GI tract**—nausea, vomiting, abdominal pain, diarrhoea (rarely pseudomembranous colitis)
- **CNS**—headache, dizziness, sleep disorders
- **Allergic**—fever, rash, anaphylaxis, photosensitivity and pruritus
- **Kidneys**—rise in blood urea and S. creatinine
- **Liver**—rise in serum transaminases and bilirubin
- **Blood**—eosinophilia, leucopenia, thrombocytopenia and altered prothrombin concentration

##### Less common

- Loss of appetite
- Disturbance of vision, taste and smell
- Hypoglycaemia, renal and hepatic impairment
- Restlessness, depression, hallucinations and confusion
- Raised intracranial tension

*Note:* The drug should be discontinued if mental, neurological or hypersensitivity reactions occur.

### Nitroimidazoles

#### Action

They have bactericidal activity against anaerobic bacteria and are amoebicidal drugs.

#### Preparations

- Metronidazole (oral and injectable)
- Tinidazol (oral)
- Secnidazol (oral)

- Satronidazole (oral)
- Ornidazole (oral).

### Uses

1. They are principally used for infections caused by anaerobic bacteria such as Vincent's angina (purulent gingivitis) and pelvic inflammatory disease, lung infection e.g. bronchiectasis.
2. Nonspecific vaginitis or trichomoniasis.
3. They are useful for intestinal and extra-intestinal amoebic infection, specifically used for amoebic liver abscess.
4. They are useful against giardiasis.
5. They are used for intra-abdominal infection, peritonitis, genital or puerperal sepsis.

### Contraindications

- 1st trimester of pregnancy, blood dyscrasias, lactation, hypersensitivity and neurological disorders

### Drug Interactions

- Alcohol (antabuse effect or disulfiram-like reactions)
- Anticoagulants, phenobarbitone, phenytoin, disulfiram

### Side Effects

- Abdominal distress, furred tongue, pseudo-membranous colitis (rare) stomatitis, glossitis (occasional), unpleasant metallic taste, neutropenia, urticaria, angioedema, CNS disturbances, dark urine, neuropathy and epileptiform seizures on long-term use.

### Indications of metronidazole infusion (500 mg/100 ml bottle)

- Anaerobic infection i.e. gut perforation, peritonitis post-puerperal sepsis
- Amoebic liver abscess if patient is not taking orally
- Antibiotic prophylaxis for surgery  
Dose: 100 ml (500 mg) 8 hourly in adults and children above 12 yrs.  
Below 12 years—7.5 mg/kg 8 hourly

- For *prophylaxis*, for vascular, urological, biliary tract surgery  
500 mg I.V infusion on induction only  
For appendicectomy and colorectal surgery  
500 mg I.V on induction plus 8 and 16 hours postoperatively

## Antitubercular Drugs

### First line (Table 3.40)

- Isoniazid
- Rifampicin
- Pyrazinamide
- Ethambutol
- Streptomycin (injectable)

### Second line

- PAS (paraminosalicylic acid)
- Ethionamide
- Cycloserine
- Kanamycin, amikacin, capreomycin
- Thiacetazone
- Rifabutin
- Quinolones (ciprofloxacin, ofloxacin and sparfloxacin)

**First line drugs being** most effective are a necessary component of any short-course therapeutic regimen, while second line drugs are less effective than first line and much more frequently elicit severe reactions. They are used only for treatment of patients with tuberculosis resistant to first-line drugs.

### Treatment regimen

1. Pleuropulmonary tuberculosis

A short course regimen

- a. Initial phase (2 months)—4 drugs
  - Rifampicin (450 mg)
  - Isoniazid (300 mg)
  - Pyrazinamide (1.5 g)
  - Ethambutol (800 mg)

*Note:* Initial phase (intensive phase) is designed to reduce the population of viable bacteria as rapidly as possible and to prevent emergence of drug resistant bacteria.



**Table 3.40:** Common antitubercular drugs

Drug	Mechanism of action	Side effects	Dose	Management in case of toxicity
1. Isoniazid (both oral and injectable)	It is both bacteriostatic and bactericidal drug It is bacteriostatic against resting bacilli and bactericidal against rapidly multiplying organisms both extracellularly and intracellularly	<ul style="list-style-type: none"> <li>Hepatotoxicity</li> <li>Peripheral neuropathy</li> <li>Rash and fever</li> <li>Acne</li> <li>Anaemia</li> <li>Arthritic symptoms</li> <li>SLE like syndrome</li> <li>Optic neuropathy, seizures and psychiatric symptoms</li> </ul>	1. Usual dose 300 mg (5 mg/kg) in adults In children: 10-15 mg/kg with maximum of 300 mg  2. For intermittent therapy, a maximum dose of 900 mg twice or thrice a week is used with vitamin B <sub>6</sub>	<ul style="list-style-type: none"> <li>Limit alcohol consumption</li> <li>Monitor SGPT and hepatitis symptoms</li> <li>Stop the drug at first symptom of hepatitis (nausea, vomiting, anorexia and flu-like symptoms)</li> <li>Concomitant administration of vit B<sub>6</sub> reduces the incidence of peripheral neuritis, optic neuritis and seizures</li> <li>Now-a-days all oral packs of anti-tubercular drugs incorporate vit B<sub>6</sub></li> <li>Limit alcohol consumption</li> <li>Monitor SGPT and hepatitis symptoms</li> <li>Reassure the patient that dark urine is due to drug itself</li> <li>Stop the drug if symptoms of hepatitis or jaundice develops.</li> </ul>
2. Rifampicin (oral)	i. It has both intracellular and extracellular bactericidal activity i.e. blocks RNA synthesis by inhibiting DNA dependent RNA polymerase  ii. It is also effective against a wide spectrum of gram-positive and gram-negative organisms	<ul style="list-style-type: none"> <li>Hepatotoxicity</li> <li>Rash</li> <li>Flu-like syndrome</li> <li>Red-orange coloured urine</li> <li>Drug interaction</li> </ul>	Adult: 450-600 mg (10 mg/kg) daily or twice a week children. 10-20 mg/kg	<ul style="list-style-type: none"> <li>Limit alcohol consumption</li> <li>Monitor SGPT and hepatitis symptoms</li> <li>Reassure the patient that dark urine is due to drug itself</li> <li>Stop the drug if symptoms of hepatitis or jaundice develops.</li> </ul>
3. Pyrazinamide (oral)	<ul style="list-style-type: none"> <li>Bactericidal drug, used in short-course therapy for tuberculosis. It has excellent CSF penetration, hence, a preferred drug in tubercular meningitis</li> </ul>	<ul style="list-style-type: none"> <li>Hepatotoxicity</li> <li>Hyperuricaemia</li> <li>Polyarthralgias</li> </ul>	Adults: 1.5 g to 2 g daily (15 to 30 mg/kg)	<ul style="list-style-type: none"> <li>Monitor SGPT and hepatitis symptoms</li> <li>Limit the dose to 15-30 mg/kg</li> <li>Monitor uric acid levels in patients of gout or renal failure</li> </ul>
4. Ethambutol (oral)	Bacteriostatic against rapidly growing mycobacterium	<ul style="list-style-type: none"> <li>Retrobulbar optic neuritis (dose related)</li> <li>Hyperuricaemia (rare)</li> </ul>	Adults: 15 mg/kg as a single dose daily For retreatment 25 mg/kg daily for 2 months then 15 mg/kg daily For intermittent therapy 50 mg/kg twice a week	<ul style="list-style-type: none"> <li>Avoid in children due to its visual toxicity</li> <li>Use the lowest dose 15 mg/kg/day</li> <li>Monitor visual acuity (eye chart) and red-green colour vision (ishihara colour chart/book) monthly, stop the drug at first change in vision</li> <li>Limit the dose and duration of therapy as far as possible</li> <li>Avoid daily therapy in old persons (&gt; 60 yrs)</li> <li>Monitor blood urea and serum creatinine levels</li> <li>Ask daily for symptoms of ototoxicity i.e. tinnitus, vertigo, dizziness and decreased hearing</li> <li>Perform audiometry if possible before and during course of therapy if needed</li> <li>Stop the drug at first development of adverse effect</li> </ul>
5. Streptomycin, amikacin, capreomycin	These drugs inhibits bacterial protein synthesis (bactericidal) for rapidly dividing extracellular mycobacteria. These drugs poorly diffuse into CSF	<ul style="list-style-type: none"> <li>Ototoxicity</li> <li>Renal toxicity</li> <li>Less common are i.e. peri-oral paraesthesias, eosinophilia, rash and drug fever</li> </ul>	Adults: 0.5 to 1.0 g (10-15 mg/kg) daily or five times a week Children: 20-40 mg/kg with a maximum of 1.0 g/day	<ul style="list-style-type: none"> <li>Limit the dose and duration of therapy as far as possible</li> <li>Avoid daily therapy in old persons (&gt; 60 yrs)</li> <li>Monitor blood urea and serum creatinine levels</li> <li>Ask daily for symptoms of ototoxicity i.e. tinnitus, vertigo, dizziness and decreased hearing</li> <li>Perform audiometry if possible before and during course of therapy if needed</li> <li>Stop the drug at first development of adverse effect</li> </ul>

b. Continuous phase ( 4 months). Two drugs used are”

- Rifampicin (450 mg)
- Isoniazid (300 mg)

2. Extrapulmonary tuberculosis (bone and joint, meningitis, pericardial disease)

The continuous phase in these type of tuberculosis is extended up to 1 year or more while initial phase is same.

#### Treatment During Special Circumstances

Although clinical trials of extrapulmonary tuberculosis are limited, therefore, the available data indicate that all forms of tuberculosis can be treated with short course 6 month regimen used for pulmonary tuberculosis. However, the American Academy of Paediatrics recommends that children with bone and joint tuberculosis, tubercular meningitis, or miliary tuberculosis receive a minimum of

12 months of treatment. Now-a-days it is applicable to adults also.

1. *Renal failure:* As a rule patient with renal failure should not receive aminoglycosides as they are nephrotoxic. Ethambutol in renal failure should be used only if serum levels can be monitored. Isoniazid, rifampicin and pyrazinamide may be given in the usual dosage in cases with mild to moderate renal failure but dosage of isoniazid and pyrazinamide should be reduced for all patients with severe renal failure except those undergoing haemodialysis.
2. *Hepatic disease:* The majority of first line antitubercular drugs i.e. isoniazid, rifampicin and pyrazinamide being hepatotoxic should be avoided in hepatic disease. Patients with severe hepatic disease may be treated with streptomycin and ethambutol and, if required, with isoniazid and rifampicin under close

**Table 3.41:** Recommended regimens for the treatment of tuberculosis

Indication	Initial phase (Bactericidal phase)		Continuation phase (sterilisation phase)	
	Duration (months)	Drugs	Duration (months)	Drugs
New smear or culture positive case	2	HRZE	4	HR*
New culture negative case	2	HRZE	2	HR*
Intolerance to H	2	RZE	7	RE
Intolerance to R	2	HES (± 2)	16	HE
Intolerance to Z	2	HRE	7	HR
Pregnancy	2	HRE	7	HR
Failure and relapse †	—	—	—	—
Standard retreatment (susceptibility testing not available)	3	HRZES ‡	5	HRE
Resistance to H+R	Throughout (12-18)	ZE + 0 + S (or another injectable drug)	—	—
Resistance to all first line drugs	Throughout (24)	Injectable agent x + 3 of these 4: ethionamide, cycloserine, PAS, 0	—	—

All drugs can be given daily or intermittently three times a week throughout or twice a week after initial phase of daily therapy. Regimen is tailored according to the results of drug susceptibility test.

‡ streptomycin treatment should be discontinued after 2 months

x Amikacin, kanamycin or capreomycin (all injectable aminoglycosides). Treatment with all of these agents should be discontinued after 2 to 6 months depending on the response and patient's tolerance.

Abbreviation

H = Isoniazid, R = Rifampicin, Z = Pyrazinamide, E = Ethambutol, S = Streptomycin, O = Ofloxacin, PAS = Para-aminosalicylic acid

supervision. The use of pyrazinamide by patients with liver cell failure should be avoided.

3. *HIV or AIDS*: Patients with HIV or AIDS appear to respond well to standard 6 months therapy, although treatment may need to be prolonged if the response is suboptimal.
4. *Pregnancy*: The regimen of choice for pregnant women is 9 months of treatment (HRE for 2 months and HR for 7 months). Streptomycin is contraindicated during pregnancy as it causes 8th nerve damage in foetus. Pyrazinamide should be avoided during pregnancy.
5. *Lactation and breast feeding*: Treatment of tuberculosis is not a contraindication to breast feeding; most of the drugs administered will be present in small quantities in breast milk, but their concentration will be too low to provide any benefit or damage.

#### *Preventive of tuberculosis*

It includes:

- i. Treatment of infectious cases with appropriate therapy until cure.
- ii. BCG vaccination
- iii. Preventive chemotherapy

#### *BCG Vaccination*

BCG vaccine was derived from a attenuated strain of *M. Bovis* and was first administered in human in 1921. Many BCG vaccines are available worldwide but vaccine efficacy varies from 80% to nil. A Cohort study conducted in areas where infants are vaccinated at birth has found higher rates of efficacy in the protection of infants and young children from serious forms of tuberculosis i.e. tubercular meningitis and miliary tuberculosis.

BCG vaccine is recommended routinely at birth in countries with high tuberculosis prevalence. In countries such as USA where it is not recommended for routine use, the vaccination is indicated only for PPD negative infants and children who are at high risk of intimate or prolonged exposure to patients with tuberculosis and who cannot take prophylactic isoniazid.

BCG vaccination is safe. The local tissue response begins 2-3 weeks after vaccination with scar formation and healing occurs within 3 months. Side effects include;

ulceration at vaccination site and regional lymphadenitis, osteomyelitis (rare), disseminated BCG infection in HIV patients.

#### *Preventive Chemotherapy*

It is a major component of tuberculosis control in USA, involves the administration of isoniazid to persons with latent tuberculosis and a high risk of active disease. It is recommended that 6-12 months course of isoniazid reduces risk of active tuberculosis in infected people by 90% or more. In the absence of re-infection, the protection is life-long. It has now been shown that isoniazid prophylaxis reduces rates of tuberculosis among person with HIV infection.

For prophylaxis, candidates are identified by PPD skin testing (Mantoux test 5 units of PPD intradermal). The positive reactions for close contacts of infectious cases, person with HIV infection, and previously untreated persons whose X-ray is consistent with healed tuberculosis are considered for prophylaxis if an area of induration is 5 mm in diameter at 48 to 72 hours (Table 3.42). A 10 mm cut off is used to define positive reactions in most other persons at-risk. For persons with low risk of developing tuberculosis, if infected, a cutoff of 15 mm is used.

#### *Contraindications for Prophylaxis*

- Presence of active liver disease
- Older patients
- Alcoholics

#### *Drug Resistant Tuberculosis*

Resistance to individual drug arises by spontaneous point mutation in the mycobacterial genome which occurs at low rate. There is no cross resistance among the commonly used anti-tubercular drugs. The development of drug resistance is invariably the result of monotherapy i.e. patient is not taking the two initial drug or poor compliance of the patient to properly prescribed therapy either due to poverty or ignorance. Drug resistance may be primary (a patient who has not been previously treated) or acquired (during the course of treatment with inappropriate regimen). Multidrug resistant tuberculosis or isoniazid/rifampicin resistant tuberculosis is emerging

**Table 3.42:** Recommendations for isoniazid prophylaxis (American Thoracic Society and the Centre for Disease Control and Prevention 1994)

<i>Risk group</i>	<i>Mantoux test (mm at 48-72 hr)</i>	<i>Duration of treatment (months)</i>
• HIV infected persons	$\geq 5^*$	12
• Close contacts of tuberculosis patients	$\geq 5^\dagger$	6 (9 for children)
• Persons with healed fibrotic lesion at chest X-ray	$\geq 5$	12
• Recently infected persons	$\geq 10$	6
• Persons with high risk medical conditions (DM, prolonged steroids therapy, other immunosuppressive therapy, haematological or RES disease, drug abuser, end stage renal disease etc.)	$\geq 10$	6-12
• High risk group < 35 yrs of age $\ddagger$	$\geq 10$	6
• Low risk group (< 35 yrs)	$\geq 15$	6

\* Anergic HIV infected persons with an estimated risk of tuberculosis of 10% may also be considered candidates

$\dagger$  Tuberculin negative contacts especially children should receive prophylaxis for 2 or 3 months after contact ends and should be retested (Mantoux test). Those whose results remain negative should discontinue prophylaxis.

$\ddagger$  It includes persons born in high-prevalence countries, members of medically underserved low-income populations and residents of long-term-care facilities.

Isoniazide is administered in a dose of 5 mg/kg/day (upto 300 mg) or 15 mg/kg (upto 900 mg) twice a week for 6 to 12 months; the longer course is recommended for persons with HIV infection and for those with abnormal chest X-ray.

fast but can be prevented by adherence to the principles of sound therapy; the inclusion of at least two bactericidal drugs to which the organism is susceptible. In clinical practice, five drugs are commonly used in the initial phase.

The treatment of individual drug resistant tuberculosis is given in the Table 3.41. For strains resistant to isoniazid and rifampicin, combination of ethambutol, pyrazinamide and streptomycin is used and if there is resistance to streptomycin also then amikacin is used. The treatment is continued for prolonged period of 12-18 months and for at least 9 months after sputum culture conversion. Many authorities add ofloxacin to this regimen.

If there is resistant to all first-line drugs, cure may be obtained with a combination of three drugs chosen from ethionamide, cycloserine, PAS and ofloxacin plus one drug chosen from amikacin, kanamycin and capreomycin (Table 3.41). The optimal duration of therapy for MDR tuberculosis in 24 months.

### ANTI-AMOEBIC DRUGS (AMOEBICIDAL DRUGS)

The drugs used to treat amoebiasis can be classified into two groups depending on the site of action.

- Luminal amoebicides:** They are poorly absorbed and reach higher concentrations in the intestines. Their activity is limited to cysts and trophozoites close to mucosa. The drugs are;

- Iodoquinol
- Paromomycin
- Diloxanide furoate

#### *Indications (Table 3.43)*

- Eradication of cysts in patients with amoebic colitis or a liver abscess
  - Treatment of asymptomatic carriers
- Now-a-days probes are available for differentiation of nonpathogenic from pathogenic cysts, however, it is prudent to treat asymptomatic individuals who pass cysts.

**Table 3.43:** Drug therapy for amoebiasis

- 1. Asymptomatic carrier (luminicidal agents)**
  - Iodoquinol (650 mg tab): 650 mg bid for 20 days
  - Iodochlorohydroxyquine (250 mg tab): 500 mg tid for 10 days
  - Diloxanide furoate (500 mg tab): 500 mg tid for 10 days
  - Paromomycin (250 mg tab): 500 mg tid for 10 days
- 2. Acute amoebic colitis (amoebic dysentery)**
  - Metronidazole (200 or 400 mg tab or 200 mg bottle for infusion): 400-800 mg orally or 200 mg IV infusion tid for 5-10 days  
or
  - Tinidazole (300 or 600 mg tab): 600 mg bid orally for 10 days  
*plus*  
Luminal agent as given above. Now-a-day combinations of oral metronidazole or tinidazole with diloxanide furoate are available
- 3. Amoebic liver abscess**
  - Metronidazole: 800 mg oral or 200 mg IV tid for 5 to 10 days  
or
  - Tinidazole: 600 mg bid orally for 10 days or 2.0 g oral as single dose  
or
  - Secnidazole: 2.0 g oral as single dose  
*plus*  
Luminal agent (diloxanide furoate 500 mg tid × 10 day)

ii. **Tissue amoebicides:** They reach higher concentration in blood and tissues after oral or parenteral administration. The drugs are nitroimidazole compounds;

- Metronidazole (oral and IV)
- Tinidazole
- Secnidazole
- Satronidazole
- Ornidazole

*Indications (Table 3.43)*

- Patient with amoebic colitis should be treated with I.V or oral metronidazole (400-800 mg tid for 5-10 days orally) or tinidazole (600 mg bid for 5 days orally) or ornidazole (400 mg bid for 5 days)
- For giardiasis, oral metronidazole 200-400 mg tid for 5-10 days
- Amoebic liver abscess. Metronidazole (oral or IV) is the drug of choice. The usefulness of

nitroimidazole in single-dose or abbreviated regimens is important in endemic areas where access to hospitalization is limited

### Infection by Free Living Amoebas

Genera include:

1. Acanthamoeba
2. Naegleria

### Naegleria Infection

*Source of infection:* Lakes, taps, hot springs, swimming pools, heating and air-conditioning units and even from the nasal passages of healthy children.

*Portal of entry:* Nasal route

*Infecting agent:* Infection follows the aspiration of water contaminated with trophozoites or cysts or the inhalation of contaminated dust.

*Disease:* Amoebic meningoencephalitis

*Diagnosis*

- CSF shows elevated proteins and low sugar. The CSF pressure is elevated with high WBC count (upto 20,000 cells/ml)
- Detection of mobile trophozoites in wet mounts of fresh CSF

*Treatment* High doses of amphotericin B and rifampicin may be used but prognosis is poor.

### Acanthamoeba Infection

*Source of infection*

The primary focus lies in the sinuses, skin or lungs.

*Mode of spread:* Haematogenous

*Clinical manifestations*

1. Granulomatous amoebic encephalitis
2. Keratitis

*Predisposing factors* It occurs typically in chronically ill or debilitated patients. Risk factors include lymphoreticular disorders, chemotherapy, steroids therapy, SLE and AIDS.

*Diagnosis*

- The syndrome mimics a space occupying lesion



- CT scan reveals cortical and subcortical lesions of decreased density consistent with embolic infarct
- CSF is having elevated pressure, hence, its examination may not be indicated in all patient; wherever it is done, trophozoites may be isolated on fresh mount of CSF

## ANTIMALARIAL DRUGS

The properties of antimalarial drugs are summarized in the Table 3.45.

### Treatment Goals

1. To suppress acute proxysm of uncomplicated malaria.
2. Radical cure to prevent relapse except in falciparum infection. Primaquine is the only drug used for this purpose.

### Indications of Antimalarials

- Treatment of uncomplicated and complicated malaria
- Eradication of malarial parasite (radical cure)
- Prevention and prophylaxis of malaria. Drug used for prophylaxis are given in the Table 3.44
- Antimalarial chloroquine is also used in treatment of amoebic liver abscess, as a disease modifying agent in rheumatoid arthritis (DMARD) and in skin lesions of systemic lupus erythematosus

### Treatment of Malaria

1. *Uncomplicated malaria (acute attack)*
  - Relief of fever by using antipyretic (paracetamol) and tepid sponging

### Box 3.22: Treatment of uncomplicated malaria

Oral chloroquine 600 mg base (10 mg/kg) followed by 300 mg (5 mg/kg) after 6 hr and then 150 mg twice a day for 2-3 days  
plus  
Primaquine 15 mg daily for 14 days is added for radical cure for patients with *P. ovale* or *P. vivax* infection after laboratory tests for G6PD deficiency have been proved negative.

### Box 3.23: Treatment of severe malaria

For severe malaria or patient is unable to take oral drug, chloroquine 300 mg base (5 mg/kg) by constant rate infusion over 4-8 hrs followed by three 8 hours infusions of 5 mg/kg (300 mg base) each

- Infection due to *P. vivax*, *P. ovale* and *P. malariae* and known strains of *P. falciparum* should be treated with oral chloroquine (Box 3.22)
2. For severe malaria or when patient is not able to take medicine orally then injectable dose of chloroquine (Box 3.23) may be given initially followed by oral treatment as soon as patient improves and start taking orally.

### Treatment of Chloroquine Resistant Malaria (Table 3.44)

In areas of chloroquine resistant strains, a combination of sulfadoxine and pyrimethamine may be used. When there is resistance to this combination as well, either quinine *plus* tetracycline/or doxycycline or mefloquine or artesunate/artemether should be used. Tetracycline and doxycycline cannot be given to pregnant women or

**Table 3.44:** Recommended dosage of anti-malarial drugs used in chloroquine resistant cases

Drug	Uncomplicated malaria (oral)	Complicated malaria (parenteral)
Tablet of sulphadoxine (500 mg) plus pyrimethamine (25 mg) (combination)	2 tablets as single oral dose	—
Mefloquine	<ul style="list-style-type: none"> <li>• For semimmune: 15 mg/kg base as a single dose</li> <li>• For resistant or nonimmune case; 15 mg/kg followed by second dose of 10 mg/kg after 8-12 hrs</li> </ul>	—
Quinine	<ul style="list-style-type: none"> <li>• 600 mg (10 mg/kg) at 8 hours intervals daily for 7 days combined with tetracycline 250 mg qid or doxycycline 3 mg/kg (200 mg) once daily</li> </ul>	<ul style="list-style-type: none"> <li>• 20 mg/kg IV infusion over 4 hours than 10 mg/kg after every 8 hours till patient starts taking orally.</li> </ul>
Artesunate or Artemether	<ul style="list-style-type: none"> <li>• Two doses of 100 mg (3 mg/kg) on the 1st day followed by 50 mg (1 mg/kg) twice daily on the following 4-6 days. Total dose is 10 mg/kg or 600 mg</li> </ul>	<ul style="list-style-type: none"> <li>• 120 mg (2.4 mg/kg) IV or IM stat followed by 60 mg (1.2 mg/kg) daily for next 4 days</li> </ul>

Table 3.45: Properties of antimalarial drugs

Drug(s)	Pharmacokinetics	Action	Minor side effects	Major side effects
Quinine, quinidine	Good oral and IM absorption	Acts mainly on trophozoite stage of all malarial species in blood, kills the gametocytes of <i>P. vivax</i> , <i>P. ovale</i> and <i>P. malariae</i> . No action in liver stages	<ul style="list-style-type: none"> <li>Bitter taste,</li> <li>Cinchonism,</li> <li>Tinnitus</li> <li>Heating loss</li> <li>Nausea, vomiting</li> <li>Postural hypotension</li> <li>QT prolongation on ECG</li> </ul> Rare <ul style="list-style-type: none"> <li>Diarrhoea, rash and visual disturbance</li> </ul>	Common <ul style="list-style-type: none"> <li>Hypoglycaemia</li> </ul> Rare <ul style="list-style-type: none"> <li>Hypotension, blindness, deafness, cardiac arrhythmias</li> <li>hemolytic anaemia, thrombocytopenia</li> <li>cholestatic jaundice, neuromuscular paralysis</li> </ul>
Chloroquine	Good oral absorption, very rapid IM and SC absorption	Similar to quinine but more rapid	Bitter taste, nausea, dysphoria, pruritus postural hypotension Rare Accommodation difficulties, rash	Acute <ul style="list-style-type: none"> <li>Hypotension or shock (IM)</li> <li>Cardiac arrhythmias</li> <li>Neuropsychiatric reactions</li> </ul> Chronic <ul style="list-style-type: none"> <li>Retinopathy</li> <li>Skeletal and cardiac myopathy</li> <li>Neuropsychiatric reactions, convulsions</li> </ul>
Mefloquine	Adequate oral absorption. No parenteral prep.	As for quinine	Nausea, giddiness, dysphoria, confusion  Sleeplessness, nightmares GI intolerance, discolouration of teeth, deposition in growing bones, photosensitivity, moniliasis, benign raised intracranial hypertension	Renal failure in patients with impaired renal functions
Tetracyclines	Excellent absorption	Weak antimalarial, should not be used alone for treatment	Diarrhoea	Prolonged QT on ECG, AV conduction delay, cardiac arrhythmias
Halofantrine	Variable absorption	As for quinine, but more rapid	Fever and reduction in reticulocyte count	Neurotoxicity reported in animals but not in humans
Artemisinin derivatives, artemether, artesunate	Good oral absorption variable in IM absorption	Broader range, specificity and more rapid action than other drugs	Well tolerated	Megaloblastic anaemia, pancytopenia, pulmonary infiltrates
Trimethoprim	Good oral absorption variable IM absorption	<ul style="list-style-type: none"> <li>Acts on the mature forms at blood stages</li> <li>Casual prophylactic</li> </ul>	Mouth ulcers and alopecia (rare)	Megaloblastic anaemia
Proguanil (chloroquanil)	Good oral absorption	<ul style="list-style-type: none"> <li>Casual prophylactic drug, not used for treatment</li> </ul>	Nausea, vomiting diarrhoea, abdominal pain, hemolysis, methaemoglobinaemia	Massive haemolysis in patients with G6 PD deficiency
Primaquine	Complete oral absorption	<ul style="list-style-type: none"> <li>Radical cure</li> <li>Some activity against blood stage infection, used to eradicate exoerythrocytic (hepatic) forms of <i>P. vivax</i> and <i>P. ovale</i> and to prevent relapses</li> <li>Kills gametocytes of <i>P. falciparum</i></li> </ul>		

## Note

- Tetracycline and doxycycline should not be used in pregnancy and in children below 8 years
- Halofantrine should not be used by patients with long QT intervals or known conduction disturbances or in those taking a drug that affect ventricular repolarisation i.e. quinine/quinidine, mefloquine, chloroquine, neuroleptics, tricyclic antidepressants, terfenadine or astemizole

to children below 8 yrs of age. Recommended dosage of drugs used in chloroquine resistant malaria and severe malaria are given in the Table 3.44.

#### *Chemoprophylaxis for Malaria*

Antimalarial prophylaxis is still a matter of controversy. Chemoprophylaxis is never entirely reliable and malaria remains in differential diagnosis of fever in patients who travelled to endemic areas, even if they are taking prophylactic antimalarial drugs.

Recommendations for prophylaxis depend on:

- i. A knowledge of local patterns of plasmodium sensitivity to drugs.
- ii. Chances of acquiring malarial infection.

#### *Indications*

1. All pregnant women at risk should receive prophylaxis.
2. Antimalarial prophylaxis should be considered for children between the ages of 3 months and 4 years in areas where malaria causes high mortality in childhood.
3. Children born to nonimmune mothers in endemic areas should receive prophylaxis from birth.
4. Travellers visiting the endemic areas of malaria. They should start taking antimalarial drugs at least 1 week before departure to endemic areas and continue for 4 weeks after the traveller has left the endemic area.

#### *Drugs (Table 3.45)*

1. Chloroquine remains the drug of choice for prevention of infection with drug sensitive *P. falciparum* and with the other human malarial species. It is well tolerated, cheap and safe during pregnancy. The side effects of the drug are depicted in Table 3.43.
2. Mefloquine has become the antimalarial prophylactic agent of choice for much of the tropics because it is effective against chloroquine and multidrug resistant *falciparum* malaria. It is also well tolerated drug but is costly.
3. Doxycycline is an effective alternative to mefloquine.
4. In the past, pyrimethamine and proguanil have been administered widely, but resistant strains of both *P. falciparum* and *P. vivax* have limited their use.

Proguanil is considered the safest drug during pregnancy. The prophylactic use of pyrimethamine and sulfadoxine is not recommended because of severe side effects.

5. Recently daily primaquine (8-aminoquinoline used for radical cure) has been found effective for prophylaxis of *P. falciparum* and *P. vivax* malaria, further studies are needed for confirmation.

The drugs used and their dosages for chemoprophylaxis of malaria are summarised in Table 3.46.

#### *Multidrug Resistant Malaria*

Drug used are:

1. Mefloquine
2. Artemisinin and derivatives (artemether and artesunate).

#### *Complications of Malaria*

These are commonly observed with *falciparum* infection.

1. Cerebral malaria
2. Black-water fever. This is common due to drugs used in malaria rather than malaria itself.
3. Acute renal failure (ARF)
4. Granulomatous hepatitis
5. Hypoglycaemia (may be quinine-induced)
6. Haematological abnormalities—anaemia, thrombocytopenia, pancytopenia, DIC
7. Aspiration pneumonia
8. Lactic acidosis
9. Noncardiogenic pulmonary oedema

#### **Q. What are the features of severe *falciparum* infection (> 20% RBCs are parasitised)?**

**Ans.** The features are;

- **CNS**—Cerebral malaria (coma, convulsions)
- **Renal**—Blackwater fever (haemoglobinuria) and acute tubular necrosis
- **Blood**—Anaemia, thrombocytopenia, pancytopenia and DIC
- **Respiratory**—ARDS
- **Metabolic**—Hypoglycaemia (children), metabolic acidosis
- **Liver**—Jaundice (haemolytic, hepatocellular)
- **GI tract**—Diarrhoea
- **Miscellaneous**—Shock, hyperpyrexia

**Table 3.46:** Chemoprophylaxis of malaria

Drug	Indication	Dose	
		Adult	Children
Chloroquine	Used in areas where malaria is chloroquine sensitive	300 mg base/week orally	5 mg/kg orally once a week
Mefloquine	Used in areas where there is chloroquine resistant malaria	250 mg salt/week orally	<ul style="list-style-type: none"> <li>• &lt; 15 kg (5 mg/kg)</li> <li>• 15-19 kg (1/4 tab/week)</li> <li>• 20-30 kg (1/2 tab/week)</li> <li>• 31-45 kg (3/4 tab/week)</li> <li>• &gt; 45 kg (1 tab/week)</li> </ul>
Doxycycline	An alternative to mefloquine	100 mg/day orally	<ul style="list-style-type: none"> <li>• &gt; 8 yr of age (2 mg/kg/day with maximum of 100 mg daily orally)</li> </ul>
Proguanil	Used simultaneously with chloroquine as an alternative to mefloquine or doxycycline	200 mg orally once a day in combination with oral weekly chloroquine	<ul style="list-style-type: none"> <li>&lt; 2 yr (50 mg/day)</li> <li>2-6 yr (100 mg/day)</li> <li>7-10 yr (150 mg/day)</li> <li>&gt; 10 yr (200 mg/day)</li> </ul>
Primaquine	Used for travellers only after testing for G6PD deficiency, post-exposure prevention for relapsing malaria	15 mg base orally once a day for 14 days	0.3 mg of base/kg orally once a day for 14 days

### Q. What are chronic complications of malaria in endemic areas (endemic malarial infections)?

- *Tropical splenomegaly* (hyperreactive malarial splenomegaly—an abnormal immune response to repeated malarial infections)
- *Quartan malarial nephropathy* (malarial-induced nephrotic syndrome due to soluble immune complex glomerular injury due to repeated malarial infections)
- *Burkitt's lymphoma and Epstein-Barr virus infection* due to immunosuppression induced by repeated malarial infections

## ANTIVIRAL AGENTS

**Acyclovir and Valacyclovir** (available both oral and IV preparations)

### Mechanism of action

They act by interfering with DNA synthesis. To become effective, it must first be phosphorylated by a virus-specific enzyme thymidine kinase in the virus infected cells; this process does not occur in non-infected cells. Therefore, the drug causes selective inhibition of DNA synthesis in virus-infected cells only.

### Indications

1. Herpes simplex virus (HSV) type I and II infections such as genital infections, encephalitis etc.
2. Varicella zoster (chicken pox, shingles) infections
3. Epstein-Barr virus (EBV) infections

**Note:** It does not eradicate viruses and is effective only if started at the onset of infection. It can save lives in herpes simplex and varicella-zoster infections in the immunocompromised host. It can also be given to immunocompromised patients for prevention of recurrence and prophylaxis of herpes simplex infection. It causes chromosomal breakage at high doses, hence, should be avoided during pregnancy.

Indications, route or administration and dosage are tabulated (Table 3.47).

### Valacyclovir

Valacyclovir exhibits 3-5 times more greater viability than acyclovir.

### Dose

- Oral: 1 g tid for 7 days
- IV: 5 mg/kg every 8 hours.

**Table 3.47:** Indications, route of administration and dosage of acyclovir

Infection	Route	Dosage	Comment
1. Varicella			
• Immunocompetent host	Oral	20 mg/kg (max 800 mg) 4 or 5 times a day	Treatment benefits reported if started within 24 hours of rash
• Immunocompromised host	IV	500 mg/m <sup>2</sup> q 8 h for 10 days	Same
2. Herpes-simplex encephalitis	IV	10 mg/kg q 8 h for 10 days	It is a drug of choice
3. Neonatal herpes simplex	IV	30 mg/kg per day as continuous infusion over 12 hr for 14-21 days	Serious morbidity is frequent despite therapy
4. Genital herpes simplex			
• Primary (Treatment)	IV	5 mg/kg q 8 hour for 5-10 days	The IV route is preferred for severe infections or with neurological complications
	Oral	200 mg 5 times a day for 10 days	
• Recurrent (Treatment)	Oral	200 mg 5 times a day for 10 days	
5. Mucocutaneous herpes simplex in immunocompromised host			
Treatment	IV	250 mg/m <sup>2</sup> q 8 h for 7 days	Choice of route of administration depend on severity of infections
	Oral	400 mg 5 times a day for 10 days	
Prevention of recurrences during intense immunosuppression	Oral	200 mg qid	
	IV	5 mg/kg q 12 h	It is administered during period of immunosuppression e.g. antimitotic drugs or after transplantation
6. Herpes zoster infections			
Immunocompromised host	IV	500 mg/m <sup>2</sup> q 8 h for 7 day	It is effective in localised zoster, particularly when given early
Immunocompetent host	Oral	800 mg 5 times daily for 7-10 days	

### Side Effects

These are well tolerated drug with fewer side effects.

1. Renal dysfunction
2. CNS changes-lethargy and tremors

### Caution in Pregnancy

Both the drugs should be avoided during pregnancy.

### Gancyclovir

It is an analogue of acyclovir, is active against HSV and VZV and is more active than acyclovir against CMV. The mechanism of action is similar.

#### Indications

It is approved for the treatment of CMV retinitis in immunocompromised host and for prevention of CMV disease in transplanted recipients.

#### Dose

Oral 1.0 g three times a day for the period of immunosuppression

Parenteral initial therapy 5 mg/kg I.V every 12 hours for 14-21 days then 5 mg/kg per day or 5 times a week as a maintenance dose for the period of immunosuppression

*Side effects* Neutropenia and bone marrow suppression.

### Vidarabine (available as IV prep)

#### Mechanism of Action

It inhibits DNA synthesis. It is effective similar to acyclovir against HSV-1 and HSV-2, VZV and EBV.

#### Indications

Similar to acyclovir

#### Dose

10-15 mg/kg/day as constant infusion over 12 hours

#### Side effects

- **Haematological**—anaemia, leucopaenia, thrombocytopenia
- **Neurotoxicity**—neuropathy



**Ribavirin (Aerosolised, oral and IV prep)**

It inhibits wide range of DNA and RNA viruses.

*Indications*

1. It has been used to treat respiratory syncytial virus (RSV) infections in infants and less extensively to treat parainfluenza virus infections in children and influenza virus A and B infections in adults. Aerosolised ribavirin has been licensed for treatment of bronchiolitis in infants.
2. Acute hepatitis
3. Herpes virus infections

*Dose* Oral 200 mg 4 times daily for 3-5 days in adults and 10 mg/kg/day in children.

*Side effects* Hypotension, cardiac arrest and respiratory effects.

*Contraindications* Pregnancy, severe hepatic and renal impairment.

**Amantadine and Rimatadine (Oral prep. only)***Mechanism of Action*

They inhibit viral replication probably by preventing uncoding of the infecting virus particles.

*Indications*

- They are used for the prophylaxis and treatment of influenza A virus.
- Amantadine is used for treatment of parkinsonism.

*Dose Adult:* 200 mg/day orally for period at risk (2-3 weeks) if used for prevention and for 5 to 7 days if used for treatment

*Children:* 9 yr (5 mg/kg/day max. upto 150 mg/day)

*Side effects* Livedo reticularis, peripheral oedema, rash and CNS disturbances.

*Contraindications* Pregnancy, lactation, severe renal disease, H/O convulsions or peptic ulceration.

**Interferons (Parenteral prep. only)**

Interferons ( $\alpha$ ,  $\beta$  and  $\gamma$ ) are cytokines that exhibit antiviral, immunomodulating and antiproliferative properties.

*Indications*

1. They show beneficial effects on genital warts when administered intralesionally or systemically.
2. Chronic hepatitis B
3. Chronic hepatitis C or non-A, non B

*Dosage* See the Table 3.48.

**ANTIRETROVIRAL DRUGS (ANTI-HIV DRUGS)**

The drugs used in HIV infection include;

- Zidovudine
- Stavudine
- Didanosine
- Zalcitabine
- Squinavir
- Lamivudine

*Mechanism of Action*

They inhibit the replication of HIV-1 and HIV-2 through competitive inhibition of reverse transcriptase and through chain termination of viral DNA synthesis.

*Dosage:* The drugs are discussed in brief in the Table 3.49.

*Side-effects of Nucleoside Analogues*

- **Haemopoietic**—anaemia, neutropenia, leucopenia
- **GI tract**—abdominal upset, anorexia, nausea, malaise
- **Hypersensitivity**—anaphylaxis, fever, rash
- **Neurological**—fatigue, asthenia, headache, convulsions, neuropathy, paraesthesias
- **Liver**—jaundice, hepatomegaly
- **Lactic acidosis**
- **Rare**—pancreatitis.

**VACCINES AND ANTITOXINS***Immunoglobulins*

They are used for passive immunization. The protection offered is immediate but short-lasting.

*Classes*

1. *Normal immunoglobulin*
  - i. It is prepared from pooled human plasma and are used for protection against hepatitis A and measles.

**Table 3.48:** Interferones

Disease	Drug	Route	Dose	Comment
1. Chronic hepatitis B	Interferon $\alpha 2B$	SC or IM	5 million units daily for 16 weeks	Hepatitis B antigen (HBsAg) and DNA are eliminated in 33-37% cases. Histological improvement occurs
2. Chronic hepatitis C or non-A, non B	Interferon $\alpha 2B$	SC or IM	3 million units thrice weekly for 24 weeks	Serum alanine transferase values return to normal in 40-50% cases but relapse occurs in half after stoppage of treatment

**Table 3.49:** Anti-HIV drugs

Name	Route	Dosage	Comment
<b>1. Nucleoside analogues</b>			
Zidovudine (ZDV)	Oral IV	200 mg q 8h 1-2 mg/kg q 4h	ZDV is recommended for treatment of patient with HIV infection and CD4 count of < 500/ml. Administration during pregnancy, during delivery and to new-born infants reduces the rate of potential HIV transmission. ddI is licensed for treatment of HIV patients who either do not tolerate or do not respond to ZDV. ddc is used in combination with ZDV in patients with advanced HIV infection who are not responding to ZDV as monotherapy. Otherwise also, combination of ZDV and ddc is superior to ZDV alone in patients with less advanced disease. Used for advanced HIV infection who are intolerant to or fail to respond to approved therapy. It is used in combination with ZDV or stavudine in patients with HIV infection and clinical or immunological disease progression. It is also used for hepatitis B infection.
Didanosine (ddI)	Oral	150-200 mg tablet bid	
Zalcitabine (ddc)	Oral	0.75 mg q 8h	
Stavudine (d4T)	Oral	30-40 mg bid	
Lamivudine (3TC)	Oral	150 mg bid	
<b>2. Protease inhibitor</b>			
Squidavir	Oral	600 mg bid	This is protease inhibitor and is approved for combination therapy with nucleoside analogues in advanced HIV infection

- ii. It has also been used to protect against rubella in susceptible pregnant women.
- iii. Used as long-term replacement therapy for congenital agammaglobulinaemia.
- iv. Used for the management of idiopathic thrombocytopenic purpura not responding to conventional therapy.
- v. Used for the management of Guillain-Barre syndrome either alone or with plasmapheresis

#### Preparations

Both IM and IV preparations are available.

2. **Specific immunoglobulins:** They are prepared from immunised donors or convalescent patients. They are used for protection against;
  - Hepatitis B
  - Tetanus
  - Varicella-zoster
  - Rabies

## Vaccines

They are used for induction of active immunity.

### Types

1. *Live vaccines*: These contain an attenuated strains of micro-organism intended to cause a subclinical infection. Some vaccines notably measles vaccine may cause a mild febrile illness. Viral vaccines both attenuated and inactivated virus are prepared in tissue culture (which may contain antibiotics) or in chick embryos. They are contraindicated in patients allergic to egg protein. Examples include: oral polio (sabin), MMR vaccine, BCG vaccine and typhoid vaccine (TY 21 a).
2. *Killed micro-organisms*: These vaccines contain either the intact killed organism (e.g. typhoid, pertussis or rabies) or specific antigens as in the case of influenza and hepatitis B (virus surface antigens). Examples include vaccines for Hepatitis A, pertussis, typhoid (whole cell or Vi antigen), polio (salk), meningococcal (gray A and C) pneumococcal and *H influenzae*.
3. *Bacterial toxins (toxoid vaccines)*: The inactivated bacterial toxins are used in vaccine preparations. Tetanus and diphtheria are two examples.

### Contraindications for Vaccination

1. In general, vaccination should be postponed if the subject is suffering from acute illness. Minor infection without fever or systemic upset are not contraindications.
2. Live vaccines should not be routinely used for pregnant women because of possible harm to foetus. They should also not be given to immunocompromised host i.e. HIV patients or patients receiving corticosteroids or radiotherapy or immunosuppressive drugs.
3. They should not be given to patients of malignant disease or tumours of reticuloendothelial system.

Vaccination and immunization are interchangeably used terms but vaccination refers to administration of vaccine or toxoid; whereas the immunization describes the process of inducing or providing immunity by any means whether active or passive. Thus vaccination does

### Box 3.24: Immunisation

#### 1. Available active immunisation

##### Live Vaccine

- Oral polio (sabin)
- Measles
- Mumps
- BCG
- Typhoid (TY 21a)
- Toxoids
- Diphtheria
- Tetanus
- *H. influenzae*

##### Recombinant vaccines

- Hepatitis B

##### Dead Organism

- Hepatitis A
- Pertussis
- Typhoid (whole cell and Vi antigen)
- Polio (salk)
- Influenza
- Cholera
- Meningococcus
- Rabies
- Pneumococcus

#### 2. Available passive immunisation

##### (Prepared antibody)

- DT (Diphtheria, tetanus).
- Botulism

##### Viral

- Hepatitis A and B
- Measles
- Rubella
- Rabies
- Varicella zoster

not guarantee immunisation. Active immunisation refers to induction of immunity by administration of appropriate antigens; whereas passive immunisation refers to providing temporary protection by administering exogenously produced immune substances. The examples of available active and passive immunisation are given in the Box 3.24. The immunisation schedule recommended by WHO for developing countries is depicted in Table 3.50 and prevalent in UK in Table 3.51.

### Vaccination for Dog Bite and Snake Bite

*Dog bite*: Rabies or hydrophobia is caused by rabies virus usually acquired by man from stray or domestic dog bite (unvaccinated dog). Infection can also be transmitted by some other animals such as cats, vampire bats, fox, wolf, monkeys. The disease has a long incubation period (1 month to 1 year). The disease once develops ends fatally.

### Prevention

- Local treatment of the wound is of great value and should be carried out as quickly as possible. The wound should be cleansed with soap or a detergent. Alcohol or antiseptic solution be applied to the wound

**Table 3.50:** Immunisation schedule recommended by WHO for developing countries

Age	Vaccine	Route	Efficacy (%)	Adverse events
Birth or First Contact	BCG (Bacillie-Calmette-Guerin)	Intradermal	75-86	Regional adenitis, disseminated BCG infection, osteomyelitis
6, 10, 14 weeks	DPT and OPV	I.M	90-95	Local reactions, hypersensitivity reactions to toxoid
		Oral	95	No significant reaction.
9 months	Measles, Mumps Rubella (MMR)	S.C	90-95%	Rarely vaccine-associated polio
12 months	Yellow fever in endemic area	S.C	High	Acute encephalopathy (measles)
18-12 months (second dose)	DPT and OPV			Rare parotitis or orchitis (mumps)
5 yrs (Booster dose)	DPT and OPV			Encephalitis, encephalopathy

MMR: Measles, mumps, rubella; DPT: Diphtheria, pertussis, tetanus (triple vaccine); IM: Intramuscular; SC: Subcutaneous  
OPV: Oral polio vaccine

**Table 3.51:** Immunisation schedule in UK

Age	Visits	Vaccine	Intervals
3-12 months	3	Three simultaneous administration of DPT + OPV and haemophilus influenzae type B	4 weeks (ideal start at 3 months of age) or at 3, 4 and 6th months)
12-24 months	1	MMR	
1st year at school	1	Booster DT + OPV	
10-13 years	1	BCG for tuberculin-negative	
Girls 11-13 yrs	1	Rubella vaccine	
15-19 years or	1	Rubella vaccine	
15-19 years or on school leaving	1	Td + OPV	

Abbreviation  
DPT: Diphtheria, pertussis, tetanus (triple vaccine)  
OPV: Oral polio vaccine  
DT: Diphtheria, tetanus  
Td: Tetanus, low dose diphtheria toxoid  
MMR: Measles, mumps and rubella

- Animal saliva must be wiped off from the surrounding skin
- Bleeding should be encouraged by application of a ligature
- Do not suture the wound
- An injection of tetanus toxoid should be given immediately.

**Vaccination with antirabies vaccine:** It should begin on the day of the bite and continued as recommended.

- For post-exposure case** (adults and children): Six doses of 1 ml IM each on day 0, 3, 7, 14, 30 and 90
  - For prophylaxis** (adults and children): Three dose of 1 ml each on days 0, 28, 56 (or day 0, 7, and 21 in urgent cases)
- Reinforcing vaccinations after 1 year and between 2 and 5 years.
- **Passive immunisation with antirabies antisera of either equine or human origin:** In some cases where the

**Table 3.52:** Special use vaccines

Vaccine	Type of vaccine	Route	Indications	Efficacy (%)	Side-effects
Anthrax	Inactivated avirulent bacteria	SC	High risk exposure (i.e. person in contact or involved in manufacture of animal tides, fur, bone meal wool, goat hair etc	90	No serious side effects
Tuberculosis (BCG)	Living bacteria (attenuated <i>M. bovis</i> )	ID	PPD negative persons in prolonged contact with active TB patient	75-86	Lymphadenopathy disseminated BCG infection, osteomyelitis
Hepatitis A	Killed virus antigen	IM	Traveller's or person living in high-risk areas	94	Local reaction
Cholera	Inactivated bacteria	SC or IM	Not recommended for public health use	50% (short lived)	Fever, pain and local swelling
Meningococcus A	Bacterial polysaccharide of 4 serotypes	SC	Military personnel, traveller's to epidemic areas	90%	Rare
Plague	Inactivated bacteria	IM	Laboratory workers, foresters in endemic area, travellers	90%	Local reaction, hypersensitivity
Rabies (Human diploid)	Inactivated virus	IM or ID	Travellers, laboratory workers, veterinarians	100%	Local reaction, arthropathy, arthritis, angioedema
Japanese encephalitis	Inactivated virus	SC	Travellers	80-90	Anaphylactic/severe delayed allergic reactions common, recipient to be observed for 10 days
Typhoid	Killed whole bacteria	IM	Used for travellers, contacts of carriers	50-70	Fever, local swelling and pain

**Abbreviations**

SC: Subcutaneous; BCG: Bacille-Calmete-Guerin; ID: Intradermal; IM: Intramuscular

\* Recommendations of the committee on immunisation practices, the American Academy of Paediatrics and the American College of Physicians

bite is extensive or from a suspected rabid animal, passive immunisation with human rabies immunoglobulin (HRIG) or equine rabies antisera should be done. Since equine antiserum can cause serum sickness, it is better to use human rabies immunoglobulin.

**Dose:** Half of the total dose e.g. 20 units/kg of HRIG (or 40 units/kg of equine antisera) is given by local infiltration of the wound and the rest by IM route into the gluteal region.

- Pregnancy is not a contraindication to post-exposure prophylaxis. If there is substantial risk of exposure to rabies, pre-exposure prophylaxis may be indicated during pregnancy, but in such a situation, human diploid cell vaccine should be used.

- **Medical staff:** The medical staff attending a patient of rabies or suspected to be suffering from rabies must be immunized. Four intradermal doses of rabies vaccine should be given on the same day at different sites.

The commonly employed vaccines and other side effects are depicted in Table 3.52.

## NUTRITION

### MINERALS AND VITAMINS

#### Iron

It is important mineral for synthesis of haem fraction of haemoglobin. It is also present in myoglobin and cytochrome system.



Normal serum iron (ferritin) level:

- Male 50-150 µg/L
- Female 15-50 µg/L

Transferrin iron binding capacity (TIBC):

- 300-360 µg/dl

Serum iron and iron binding capacity in different condition are given in the Box 3.25.

Iron saturation (%) = It is calculated by serum iron divided by iron binding capacity  $\times 100$ . The normal value is 30-50%. Iron deficiency states are associated with saturation  $< 20\%$ , while iron overload occurs if saturation exceeds 50 to 60%.

**Box 3.25:** Serum iron and iron binding capacity in different conditions

Microcytic hypochromic anaemia	Serum iron	Total Iron binding capacity
1. Iron deficiency anaemia	Decreased	Increased
2. Inflammatory diseases associated with anaemia	Decreased	Decreased
3. Sideroblastic anaemia	Increased	Normal
4. Thalassaemia	Normal	Normal

### Iron Deficiency Anaemia

It is microcytic hypochromic anaemia.

Other causes of microcytic hypochromic anaemia are:

- Sideroblastic anaemia
- Thalassaemia

### Iron preparations

Oral preparation (Table 3.53).

### Parenteral Preparations

1. Iron dextran injection (100 mg elemental iron)

2. Iron sorbitol citric acid complex (75 mg elemental iron)

### Indications of iron therapy

1. Increased physiological demands e.g. pregnancy, lactation, infants, children.
2. Iron deficiency anaemia due to
  - Poor intake (nutritional)
  - Malabsorption
  - Parasitic infestation e.g. hookworm disease
  - Blood loss e.g. menstrual, haematemesis, piles or haemorrhoids
3. Parenteral preparations are used (i) in patients who are unable to tolerate oral iron or who suffer from malabsorption syndrome and (ii) in patients receiving recombinant erythropoietin therapy to guarantee adequate iron delivery to support erythropoiesis

**Dose.** The amount of iron needed can be calculated as follows:

$$\text{Total dose (mg)} = \text{Body wt (kg)} \times 2.3 \times (15 \text{ minus patient's Hb in g\%}) + 500 \text{ to } 1000 \text{ mg (to replenish iron store)}$$

### Precautions

1. Iron dextran complex should be administered after a test dose of 0.5 ml and patient observed for complaints of itching, chest or back pain and breathlessness. The BP should be monitored throughout the period of administration.
2. To be given as deep intramuscular injection. Phenol free preparation of iron-dextran can be given by IV route also.
3. Side effects of parenteral therapy include anaphylactic reactions or serum sickness (fever, arthralgia, rash, malaise and lymphadenopathy).

**Table 3.53:** Oral iron preparations

Generic name	Tablet (iron content) mg	Elixir (iron content) mg	Dose
Ferrous sulphate	325(65) 195(39)	300(60) 90(18)	200-250 mg of elemental iron/day
Slow release Ferrous fumarate	525(105) 325(107) 195(64)	— — 100(33)	
Ferrous gluconate	325(39)	300(35)	

*Precautions*

1. To be given after meals to avoid GI tract symptoms.
2. Patient should not be on antacid or tetracycline therapy as they interfere its absorption.

*Side effects:* Oral preparations are safe and produce GI upset which can be minimised if iron is taken after meals.

**Vitamins**

These are organic compounds not synthesised within the body and are taken in diet. Only a small amount of vitamins is required in the diet because they are not energy yielding substances but act as catalytic co-factors for biological reactions.

*Causes of Vitamin(s) Deficiency*

- i. General malnutrition-poor intake
- ii. Increased demands during growth, pregnancy and lactation
- iii. Food-faddism: consumption of staple diet
- iv. Malabsorption; diarrhoea, parasitic infestations, etc.
- v. Haemodialysis
- vi. Parenteral nutrition
- vii. An inborn error of metabolism
- viii. High processing, boiling or other sophisticated measures may destroy vitamins.

*Diagnosis*

Biochemical means of proving vitamin deficiency, once suspected are limited and the role of vitamin deficiency in disease state is not recognised because nonspecific vitamin therapy is a common part of standard supportive care i.e. prescribed without proven deficiency. As a consequence, knowledge of manifestations of vitamin deficiency and a high degree of suspicion in appropriate

setting are essential for considering the diagnosis and demonstration of a response to replacement therapy may be the most accurate way to confirm the diagnosis.

*Hypervitaminosis*

Excess of vitamins can be consumed either as a result of indirect consequence of dietary practice or by deliberate ingestion. Excess of vitamin A and D consumption and subsequent syndromes development are well recognised; while toxicity syndromes resulting from excessive consumption of water soluble vitamins are inconsistent and less well understood.

Normal requirement of fat soluble vitamins A, D, E, and K are given in the Table 3.54.

**Vitamin A**

Sources (Box 3.26).

**Box 3.26:** Sources of Vit A

1. Animal source (vit A or retinols)
  - Milk, butter, cheese, eggs yolk, fish, liver oils etc
2.  $\beta$ -Carotene (Plant sources)
  - Carrots, dark green leafy vegetables, yellow fruits, red-palm oil etc

*Clinical significance*

1. It is an anti-oxidant vitamin along with vitamin C and E, is used to prevent acceleration of atherosclerosis e.g. diabetes, CVA, IHD etc.
2. It is used as a part of protection against epithelial cancer
3. Vit. A deficiency predisposes to infection.
4. Its requirement increases during pregnancy, lactation and growth
5. It is used for acne and other dermatological conditions
6. It must be supplemented in deficiency states.

**Table 3.54:** Requirements of fat soluble vitamins

	Vitamin A(mgRE)	Vit. D (mg)	Vit. E (mg $\alpha$ -TE)	Vit. K (mg)
Infant	375	7.5-10	3-4	5-10
Children (1-10 yrs)	400-700	10	6-7	15-30
Adult Male	1000	2.5	10	50-80
female	800	2.5	8	50-65
Lactating or pregnant womens	1000-1200	10	11	65

*Deficiency signs/symptoms*

- Night blindness
- Xerophthalmia
- Keratomalacia
- Xerosis
- Hyperkeratosis of skin
- Bitot's spot

*Prevention*

1. Pregnant women, lactating mother, growing children should be advised to take adequate amounts of dark green leafy vegetables and green or yellow fruits.
2. Controlled trials in Indonesia, Nepal, Ghana, India have shown that in communities where xerophthalmia is prevalent, a single dose of 60 mg retinol (200,000 IU of vitamin A as palmitate) to preschool children significantly reduced mortality from gastroenteritis and respiratory infections by 33%.

*Treatment*

1. Night blindness-30,000 IU of Vit A daily for 7 days
2. Corneal damage-20,000 IU/kg/day × 5 days
3. Children who are at risk for vitamin A deficiency and who develop measles should be given 200,000 IU orally each day for 2 days
4. Associated malnutrition must be treated and superadded bacterial infection should be treated with antibiotics
5. Referral to ophthalmologist is necessary for severe cases.

**Hypervitaminosis A (Vitamin A toxicity)**

Hypervitaminosis A can result from accidental ingestion of polar bear, liver by hunters or explorers, food faddism or as a side effect of inappropriate therapy

*Acute toxicity* results from ingestion of a large dose and is characterised by abdominal pain, nausea, vomiting, headache, dizziness and in infants a bulging fontanelle followed by desquamation of skin. Recovery occurs within few days

*Chronic toxicity* occurs following ingestion of large doses for prolonged periods; for example when taken for acne

or other dermatological conditions. The features include; bone and joint pain, hyperostosis, hair loss, dryness of lips, weight loss, benign intracranial hypertension and hepatosplenomegaly. Relief is prompt on withdrawal of vitamin.

**Vitamin D**

*Synthesis:* Natural form of vit D (cholecalciferol, Vit. D<sub>3</sub>) is synthesised in the skin by the action of UV light on 7-dehydrocholecalciferol. Cholecalciferol is inactive in the present form, becomes active after hydroxylation twice, first in liver and then in kidneys. The active end-metabolite formed in the kidneys is 1-25 dihydroxy-cholecalciferol. Therefore, patients with renal disease requiring vit D should have hydroxylated derivatives (alfacalcidol or dihydrocholecalciferol)

*Sources of Vit D*

1. Natural from skin.
2. Dietary-main sources include; fish liver oil (cod liver oil), fatty fish and infant milk formula fortified with Vit. D.

*Functions*

It stimulates the absorption of calcium from the small intestine and inhibits mobilisation of calcium from bone resorption.

*Deficiency syndromes*

1. Rickets in children
2. Osteomalacia in adults

*Causes of Vit. D deficiency (Box 3.27)***Box 3.27: Causes of Vit D deficiency**

1. Poor dietary intake or less synthesis through skin (common in muslim ladies using purdah).
2. Defective absorption e.g. coeliac disease in children, pancreatic or biliary duct obstruction or GI surgery.
3. Defective metabolism e.g. interference by drugs (diltiazem, rifampicin) and chronic renal failure.

*Rickets may due to;*

- i. Hypocalcaemia due to vit D deficiency

- ii. Hypophosphataemia e.g. familial, inherited or acquired renal tubular defects (Fanconi's syndrome, calcinosis, multiple myeloma, cadmium poisoning, outdated tetracyclines)

Uses of Vit. D (Box 3.28)

**Box 3.28: Uses of Vitamin D**

Deficiency state	Dose
1. Ricket	• 25-125 mg(1000-5000 IU) daily for 6-12 weeks then 200-400 IU daily orally
2. Osteomalacia	• Same dose
3. Osteomalacia due to malabsorption	• 5,000-10,000 IU orally daily and large doses of calcium OR 10,000 IU daily I.M depending on calcium and vit. D levels
4. Anticonvulsant therapy	• Add 1000 IU/day to drug therapy
5. Renal disease	• Initially alphacalcidol 0.5 µg/d or calcitriol 0.25 µg/d and increase the dose as per response (usual dose is 1µg/day for α-calcidol and 0.25-0.5 µg for calcitriol) and continue for 2-4 weeks. serum calcium levels are to be monitored
6. Refractory osteodystrophy	• 1.0-2.5 µg three times/week intravenously and in patient on dialysis titrate the response to calcium and PTH levels
7. Hyperthyroidism	• Small dose of Vit D <sub>3</sub> and calcium supplementation

#### Hypervitaminosis D (Vit D intoxication)

The symptoms include nausea, vomiting, constipation, drowsiness, dizziness and metastatic calcification; and are mainly due to hypercalcaemia. Renal damage may occur. Breast milk from women taking vit. D may cause hypercalcaemia in breast-fed infants.

#### Vitamine E (Tocopherols)

Eight naturally occurring tocopherols possess vitamin E activity and α tocopherol is widely distributed and most active of all tocopheroles.

Requirement: Adult 10-30 mg/day

**Action:** It is an antioxidant vitamin and prevents formation of toxic oxidation products.

#### Clinical Deficiency

Isolated deficiency is rare and occur with selective malabsorption of the vitamin or when an autosomal recessive mutation causes vit. E deficiency and ataxia. The manifestations of deficiency include areflexia, gait disturbance, decreased proprioceptive and vibration sense and paresis of gaze associated with posterior column degeneration.

#### Uses

1. Vitamin E deficiency due to malabsorption, cholestatic jaundice
2. Abetalipoproteinaemia
3. As an antioxidant vitamin along with vit. A or C
4. Fibrocystic breast disease
5. Empirically used for muscle cramps

Dose: 50-100 IU/day

#### Vitamin K

It is present in two forms i.e. Vit K<sub>1</sub> (Phytonadione) in green leafy vegetables and K<sub>2</sub> (menaquinone) synthesised by intestinal bacteria. It is coagulant vitamin required for the synthesis of four clotting factors i.e. II, VII, IX, X-called Vit K dependent clotting factors.

Daily requirement: 80 mg/day.

**Causes of deficiency:** Deficiency of Vit K causes haemorrhagic disease in newborn and clotting disorders in adults.

1. Primary deficiency in new born occurs due to inefficient transfer of Vit K from the mother to foetus leading to haemorrhagic disease
2. Obstructive (cholestatic) jaundice or hepatocellular failure causes decreased synthesis of vit K dependent factors leading to coagulation disorder
3. Anticoagulants i.e. warfarin and related anticoagulants antagonise vit K
4. Antimicrobial therapy (prolonged) eliminates the bacteria required for its synthesis.

Dose: Patients with PTI <70% should receive parenteral vitamin K 10 mg/day for 3-5 days till PTI becomes normal or tolerable (>70%).

### Water Soluble Vitamins

It includes: Vitamin C and B-complex group

#### Vitamin C (Ascorbic Acid)

##### Functions

1. It helps in collagen formation of connective tissue by hydroxylation of proline to hydroxyproline-the characteristic aminoacid of the collagen. By this action, it helps in healing of the wound
2. It is most effective reducing agent in aqueous phase of living tissue
3. Vitamin A, C and E are antioxidant vitamins.
4. It is anti-scurvy vitamin.

*Daily requirement:* 30-70 mg/day. Requirement increases during pregnancy and lactation.

##### Dietary sources

*Vegetable sources* e.g. guava, potatoes, cabbage, cauliflower (row) and citrus fruits.

*Animal sources* e.g. meat (liver, kidneys, fish)

##### Deficiency disease - Scurvy

##### Uses

1. Prevention and treatment of scurvy
2. As an antioxidant vitamin
3. Pregnancy and lactation
4. During trauma, surgery, burns, infections, smoking
5. Higher doses have been used in URI without much success.

##### Dose

*In adult scurvy:* 500-1000 mg two or three times a day

*In infection:* 1.0 g 2-3 times a day

*Children* <4 years: 1/4 of adult dose

5-12 years: 1/3 of adult dose

13-14 years: 1/2 of adult dose

##### Hypervitaminosis C (Vit C toxicity)

1. Large amount of iron may be absorbed and may precipitate haemochromatosis
2. Precipitate oxalate stone formation by producing oxaluria
3. Long-term use may interfere with absorption of Vit B<sub>12</sub>.

### Vitamine B Complex

It includes:

B<sub>1</sub> = Thiamine B<sub>2</sub> = Riboflavin

B<sub>3</sub> = Nicotinic acid (nicotinamide) B<sub>5</sub> = Pantothenic acid

B<sub>6</sub> = Pyridoxine

B<sub>12</sub> = Cyanocobalamin, hydroxocobalamin.

The Vit. B complex, their source, daily requirements, deficiency states and their uses are tabulated (Table 3.55).

### DRUGS USED IN RESPIRATION DISEASES

#### Anti-histamines (H<sub>1</sub> Blockers)

##### Actions

The anti-histamines block those responses to histamine that are mediated by H<sub>1</sub> receptors (bronchoconstriction, contraction of GI tract smooth muscles, vasodilation and pruritus), hence, are also called *H<sub>1</sub> blockers*. These compounds exert their actions by competitively inhibiting H<sub>1</sub> receptors. They do not prevent the release of histamine. In addition, these drugs also exert anticholinergic and antiserotonergic activity.

##### Preparations

These include *chlorpheniramine*, *brompheniramine*, *clemastine*, *cyclizine*, *cyproheptadine*, *dexchlorpheniramine*, *diphenhydramine*, *hydroxyzine*, *meclozine*, *methidiazine-pheniramine*, *promethazine*, etc.

*Acrivastine*, *cetirizine*, *loratadine*, *fexofenadine* are new antihistaminics.

##### Uses

1. Allergic conditions such as hay fever, allergic rhinitis, urticaria, contact dermatitis, pruritus.
2. Insect bites, stings and drug rashes/allergies.
3. Some e.g. cyclizine, diphenhydramine and meclizine are also used in Meniere's disease, motion sickness and other forms of vertigo, nausea and vomiting.
4. Some e.g. cyproheptadine has also been used in the treatment of migraine.
5. Injections of chlorpheniramine or promethazine are used as an adjuvant to adrenaline in the emergency



**Table 3.55:** Vitamins B complex—dietary source, daily requirement, deficiency states and indications for their use

Name	Dietary source	Daily requirement	Deficiency syndrome	Use
<p><b>Thiamine (B<sub>1</sub>)</b> It acts as an coenzyme in</p> <ul style="list-style-type: none"> <li>Decarboxylation of pyruvate to acetyl coenzyme (Kreb's cycle)</li> <li>For transketolase in hexose-monophosphate shunt</li> <li>Decarboxylation of ketoglutarate to succinate in Kreb's cycle</li> </ul>	<ul style="list-style-type: none"> <li>Wheat flour (bran), bread</li> <li>Yeast, legumes, nuts</li> <li>Oat meal or fortified cereals</li> <li>Meat</li> </ul>	1.5 mg/day	<ul style="list-style-type: none"> <li>Beri-Beri e.g. dry, wet, infantile (cerebral Beri-Beri)</li> <li>Korsakoff psychosis</li> </ul> <p><i>Causes of deficiency</i></p> <p>Alcoholism, malnutrition, malabsorption, antidiabetic therapy, dialysis, folate deficiency intake of machine-milled rice or cereals</p>	<ol style="list-style-type: none"> <li>For <i>beri-beri</i>: Initially 50 mg IM is given for several days after which it is given orally 2.5-5 mg</li> <li>For therapeutic test for beri beri; A single injection 100 mg produce a prompt relief of symptoms when beriberi is in doubt</li> <li>As a neurotropic vitamin in association with Vit B<sub>6</sub> and B<sub>12</sub> used in various types of peripheral neuropathies</li> </ol>
<p><b>Riboflavin (B<sub>2</sub>)</b></p> <ul style="list-style-type: none"> <li>As a coenzyme in oxidation-reduction reactions</li> </ul>	—	1.2-1.6 mg/day	<ul style="list-style-type: none"> <li>Sore throat, (hyperemia, oedema of oral mucous membrane, cheilosis, angular stomatitis, glossitis, seborrhoeic dermatitis and normocytic bone marrow hypoplasia)</li> </ul> <p><i>Pellagra</i> (diarrhoea, dermatitis, dementia)</p> <p><i>Cause:</i> Consumption of staple diet such as maize, jowar sorghum containing high leucine content for long period</p>	<ul style="list-style-type: none"> <li><i>In deficiency state</i> 2.5-5 mg daily orally for few days</li> </ul>
<p><b>Nicotinamide (Niacin)</b></p> <ul style="list-style-type: none"> <li>As coenzyme in; oxidation-reduction reactions as NAD and NADP</li> </ul>	Cereals	14-18 mg	<ul style="list-style-type: none"> <li>Oral niacin 10 mg/day to treat endemic pellagra</li> </ul>	
<p><b>Pyridoxin (Vit B<sub>6</sub>)</b></p> <ul style="list-style-type: none"> <li>Pyridoxal phosphate acts as coenzyme in many aminoacid metabolism e.g. transaminases, synthetases, hydroxylases</li> <li>Required for synthesis of haem precursors</li> <li>Plays a role in neuronal excitation</li> </ul>	Widely distributed in all foods e.g. meat, liver, vegetables, cereals	2 mg/day	<ul style="list-style-type: none"> <li>There is no isolated deficiency syndrome described but certain disorders depend on pyridoxine; <ul style="list-style-type: none"> <li>Infantile convulsions</li> <li>Homocysteinuria</li> <li>Sideroblastic anaemia</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>In deficiency due to pregnancy, oral contraceptives or isoniazid induced; 30 mg/day oral is sufficient</li> <li>For patients taking penicillamine, 100 mg/day</li> <li>For peripheral neuropathies in conjunction with Vit B<sub>1</sub> and B<sub>12</sub></li> </ul>
<p><b>Vitamin B<sub>12</sub> (Cyanocobalamin)</b></p> <p>Two metabolic active</p> <ol style="list-style-type: none"> <li>Methyl-cobalamin: It is a cofactor for conversion of homocysteine to methionine, hence, its deficiency results in</li> </ol>	<ul style="list-style-type: none"> <li>Fortified cereals, spinach, peas, dried beans, cauliflower, whole meal bread, vegetables</li> </ul>	<p>Adult requirement is 2 mg/day</p> <p>Children: 1.4 mg/day</p> <p>Pregnant and lactating mothers:</p>	<ul style="list-style-type: none"> <li>Pernicious anaemia</li> <li>Homocysteinemia and thrombosis of vessels</li> <li>Subacute combined degeneration of spinal cord</li> <li>Peripheral neuropathies of</li> </ul>	<p>Therapeutic preparations used are;</p> <ul style="list-style-type: none"> <li>cyanocobalamin and hydroxocobalamin</li> <li>For <i>pernicious anaemia</i></li> <li>Hydroxocobalamin parenterally as 1000 mg twice a week for 2 weeks, then 1000 mg/week for 6 weeks.</li> </ul>

Contd...

Table contd...

Name	Dietary source	Daily requirement	Deficiency syndrome	Use
dearranged folate metabolism and megaloblastic anaemia, elevation of plasma homocysteine levels that predispose to thrombosis and to some extent neurological complications ii. Adenosylcobalamin: It converts methylmalonyl coenzyme A (CoA). Lack of this factor leads to accumulation of methylmalonyl CoA and its precursors which may contribute to neurological complication		2.6 mg/day	metabolic, drug induced or idiopathic <i>Causes of Vit B<sub>12</sub> deficiency are</i> • Inadequate dietary intake • Gastrectomy (loss of intrinsic factor) • Disease of terminal ileum (loss of absorption site) • Blind loop (bacterial colonisation of small intestine with consumption of Vit B <sub>12</sub> )	Monitor the response The maintenance dose is 1000 mg IM after every 3 months throughout life • For malabsorption it is given along with an antibiotic course for short-term • For neuropathies, it is given along with B <sub>1</sub> = 100 mg B <sub>6</sub> = 50 mg B <sub>12</sub> = 1000 mg daily for 10 days <i>Note:</i> Folic acid should not be given in Vit B <sub>12</sub> deficiency with neurological features
<b>Folic acid</b> • It is an essential hemopoietic vitamin. The activity of folic acid and Vit B <sub>12</sub> is essential for normal erythropoiesis	Fortified cereals spinach, peas, beans, cauliflower, vegetables, whole bread	Adults: 100 mg/day Children: 50 mg/day Pregnant women: 400 mg/day Lactating mothers: 260 mg/day	• Megaloblastic anaemia • Tropical nutritional paraplegia • Homocysteinaemia and subsequent vascular thrombosis • Congenital neural tube defects if deficiency persists during pregnancy <i>Causes</i> • Inadequate dietary intake or alcoholism • Malabsorption • Infection • Pregnancy • Drug induced e.g. phenytoin, methotrexate, oral contraceptives, • Di Guglielmo's syndrome	<i>Uses and dosage</i> • For megaloblastic anaemia 5 mg/day for few days then 5 mg/week. Folate will aggravate the neurological complication of vitamin B <sub>12</sub> deficiency if given alone in combined deficiency. Hence, it is customary to use both simultaneously in megaloblastic anaemia • Dimorphic anaemia: It is used as an adjuvant to iron therapy • Pregnancy: Folate supplements 350 mg/day • For prevention of stroke and coronary occlusion in cases with high levels of homocysteine • Used as an adjuvant to antifolate drugs

treatment of angioedema, urticaria and systemic anaphylaxis (type 1 hypersensitivity reactions).

6. Systemic mastocytosis.

#### Contraindications

- Previous hypersensitivity
- Nursing mothers and premature or newborn infant
- Narrow angle glaucoma
- Epilepsy
- Concomitant therapy with MAO inhibitors
- Treatment of lower respiratory tract infections or acute asthmatic attacks
- Urinary retention and prostatic hypertrophy.

#### Side Effects

1. **CNS:** Mainly sedation but CNS stimulation accompanied by hallucinations and convulsions, headache, dizziness. Fever may occur after large dose in children.
2. **GI tract**, e.g. abdominal upset and distension.
3. **Blood dyscrasias**
4. **Anticholinergic effects**—dry mouth, blurring of vision
5. **Arrhythmias:** Astemizole and terfenadine prolong QT interval and are arrhythmogenic, hence, not to be used with drugs that prolong QT interval.

### Anaphylaxis and Angioedema (Type 1 Hypersensitivity Reactions)

#### Definition

The life-threatening anaphylaxis (anaphylactic shock) occurs in a sensitized human within minutes after administration of specific antigen and is manifested by laryngeal oedema, bronchospasm and hypotension or shock or vascular collapse. Cutaneous manifestations such as pruritus, urticaria, angioedema are characteristics of systemic anaphylaxis. GI tract manifestations include nausea, vomiting, crampy abdominal pain and diarrhoea.

#### Causes

1. Heterologous proteins such as hormones, enzymes, pollen extracts, food, antiserum or vaccines etc.

2. Insect bites/stings

3. Drugs

- Antibiotics (penicillins, cephalosporins, amphotericin B)
- Local anaesthetics (procaine, lidocaine)
- Iron injections
- Vitamin injections
- Heparin
- Neuromuscular blocking agents

#### Treatment

1. Make the patient to lie flat with foot end raised.
2. IV adrenaline (1:1000 sol) 0.5 to 1 ml every 10 minutes till patient improves.
3. Repeated slow IV injection of chlorpheniramine after adrenaline may be helpful and should be continued for 24 hours.
4. In the absence of adequate improvement, administer IV fluids, IV aminophylline, O<sub>2</sub> and assisted ventilation; if required, tracheostomy may be done on emergency basis especially in angioedema.
5. IV corticosteroids are of secondary help because their onset of action is delayed for few hours. They should be used simultaneously in severe reaction and shock.

### Bronchodilators

These drugs relax the bronchial mucosa and produce dilatation of bronchial system hence called *bronchodilators*. These include;

**Sympathomimetics (adrenergic stimulants)** They produce bronchodilation by stimulating  $\beta_2$  adrenergic receptors in bronchial smooth muscles. The drugs in this category include; *catecholamines* (adrenaline or epinephrine, ephedrine, isoprenaline etc), *resorcinols* (metaproterenol, terbutaline and fenoterol) and *saligenin* (albuterol or salbutamol).

The catecholamines are short-acting (30 to 90 min) and are effective only when administered by inhalational or parenteral routes. These are not  $\beta_2$  selective agent and have considerable chronotropic and inotropic effects. These are used in emergency situation of asthma and type I hypersensitivity (anaphylactic) reaction (e.g. subcutaneous or IV adrenaline 0.5 ml of 1:1000 sol or isoproterenol is used 1:200 solution by inhalation).

**Table 3.56:** Commonly used selective  $\beta_2$  stimulants

Drug	Uses	Dose	Side effects
1. Terbutaline	<ul style="list-style-type: none"> <li>Bronchial asthma</li> <li>Bronchitis</li> <li>Mucoviscidosis</li> </ul>	<ul style="list-style-type: none"> <li>Oral: 2.5-5 mg tid in adults</li> <li>Inj: 0.5-1 ml SC or IM upto 4 times a days</li> <li>Inhalation: 0.25 mg per metered dose 1-2 puffs during acute attack and then as required max 8 puffs in 24 hrs</li> <li>Nebuliser: 5-10 mg diluted and nebulised 2-4 times daily</li> </ul>	<ul style="list-style-type: none"> <li>Fine tremors</li> <li>Peripheral vasodilatation</li> <li>Hypotension</li> <li>Headache</li> <li>Palpitation</li> <li>GI upset</li> <li>Muscle clamps</li> <li>Sleep disturbance</li> <li>Hypokalaemia</li> </ul>
2. Salbutamol	<ul style="list-style-type: none"> <li>Bronchial asthma</li> <li>Chronic bronchitis or acute exacerbation of COPD</li> <li>Bronchospasms due to any other cause</li> <li>For prophylaxis of asthma</li> </ul>	<ul style="list-style-type: none"> <li>Oral: Adults 2-4 mg 3-4 times a day</li> <li>Inhalor: Adult 200-400 mcg as a single dose</li> <li>Children 200 mcg (single dose)</li> <li>For prophylaxis 400 mcg 3-4 times a day in adult and half the dose in children</li> </ul>	<ul style="list-style-type: none"> <li>GI symptoms e.g. nausea, vomiting diarrhoea</li> <li>Fine tremors</li> <li>Insomnia, hyperactivity, nervousness, headache</li> <li>Palpitation, sweating</li> <li>Peripheral vasodilatation</li> </ul>
3. Salmeterol	<ul style="list-style-type: none"> <li>Regular treatment of asthma. Note to be used in acute attack</li> </ul>	<ul style="list-style-type: none"> <li>Inhalor: Two puffs (40 mcg) twice a day (25 mcg per metered In severe cases 4 puffs bid dose) Not to be used in children</li> </ul>	<ul style="list-style-type: none"> <li>Muscle cramps (rare)</li> <li>Hypokalaemia (rare)</li> </ul>
4. Formoterol	<ul style="list-style-type: none"> <li>Regular treatment of bronchial asthma</li> </ul>	<ul style="list-style-type: none"> <li>Inhalor: <i>Adults</i>: 6 mcg/per metered dose. 1-4 puffs twice a day, titrated to the lowest effective dose</li> <li><i>Children</i>: Under 6 yrs not recommended over 6 yrs, half the adult dose</li> </ul>	Same as above

Note: Special precautions in cardiac disease, diabetes, hyperthyroidism, gastric ulcer, pregnancy, lactation, hypertension, arrhythmias, hepatic and renal impairment

*Side effects* include; tachycardia, palpitation, cardiac arrhythmias, precipitation of angina, CNS stimulation, dry mouth, sweating, headache, dizziness, nausea, vomiting, nervousness, anxiety and tremors.

The commonly used resorcinol (terbutaline) and saligenin (salbutamol) are highly selective  $\beta_2$  stimulants for respiratory tracts and are virtually devoid of significant cardiac effects except at high doses. They are active by all routes and their effects are long-lasting 4-6 hours.

#### Uses

1. Bronchospasm due to any cause e.g. allergies
  2. Bronchial asthma
  3. Chronic bronchitis or COPD
- The doses and side effects are given in the Table 3.56.

### Xanthine Derivatives

#### Actions

They produce bronchodilation by inhibiting the enzyme phosphodiesterase leading to increase in intracellular levels of cyclic AMP. In addition;

1. They are cardiac stimulants.
2. They produce diuresis
3. CNS and respiratory stimulants

*Uses and dosage* See the Table 3.57.

### Anticholinergics (Ipratropium bromide Oxitropium bromide inhalation)

Anticholinergic drugs produce bronchodilation by smooth muscle relaxation and are useful as broncho-

**Table 3.57:** Commonly used methylxanthines

Drug	Uses	Dose	Side effects
Aminophylline	<ul style="list-style-type: none"> <li>• Anaphylaxis</li> <li>• Acute asthma</li> <li>• COPD</li> <li>• Cor pulmonale</li> <li>• CHF</li> <li>• Dobutamine induced coronary steal causing ischaemia during dobutamine stress testing</li> </ul>	Adults: I.V aminophylline/theophylline 250 mg (or 6 mg/kg) as a bolus followed by 1 mg/kg/hr (250 mg over 4 hr) as slow I.V infusion for 12 hours then 250 mg as an infusion over 6 hrs for 24 hrs or as long as required	<ul style="list-style-type: none"> <li>• <i>GI tract:</i> nausea, vomiting, anorexia, epigastric pain, diarrhoea, haematemesis</li> <li>• <i>CNS:</i> headache, convulsions, insomnia</li> <li>• <i>CVS:</i> tachycardia, flushing, hypotension extrasystoles and life threatening arrhythmias</li> <li>• <i>Renal:</i> albuminuria</li> <li>• <i>Miscellaneous</i> e.g. hyperglycaemia tachypnoea</li> </ul>
Theophylline	– do –	Adults: IV dose as discussed above Oral: 300 mg 2-3 times a day	<i>Special precautions</i> Pregnancy, lactation, hyperthyroidism, gastric ulcer, myocardial insufficiency, diabetes Same as above

Note: These can be used in combination with  $\beta_2$  adenergetic stimulants.

dilators in bronchial asthma and chronic bronchitis. They may be of particular benefit for patients with co-existent heart disease in whom use of xanthine derivatives and  $\beta_2$  adrenergic stimulants may be dangerous. There is some evidence that addition of anticholinergics may enhance the bronchodilation achieved by sympathomimetic. They are slow to act (60-90 min for peak action) and are only of modest efficacy.

#### Drug and Dose

*Drug:* Ipratropium bromide inhalor 20 mcg/per metered dose.

*Dose:* Adult 1-2 inhalations 3-4 times a day.

*Side effects*—dry mouth, urinary retention, constipation, headache, nausea, throat irritation and cough.

#### Corticosteroids (Oral or Inhaled)

They are not bronchodilators but are potent anti-inflammatory agents. They prevent attacks by reducing airway hyper-responsiveness, mucosal oedema and bronchial secretions.

#### Uses

- Acute severe bronchospasm not responding to other bronchodilators
- Acute severe asthma

*Doses and drugs* (Table 3.58).

*Side effects* Read Corticosteroids.

#### Mast Cell Stabilisers (Sodium cromoglycate, Nedocromil)

##### Action

They inhibit the degranulation of mast cells, thereby preventing the release of the chemical mediators of anaphylaxis.

##### Uses

- They are most effective in atopic patients who have either seasonal or perennial airway obstruction
- Prophylactic use: When given prophylactically, they will block the acute obstructive effects of exposure (acute bronchial asthma) to antigen, industrial chemicals, exercise or cold air. They should be used intermittently before provocation of acute episode of asthma i.e. the drug to be taken 15-20 minutes before contact with precipitant.

*Doses* See the Table 3.59.

#### Antihistaminic (Ketotifen)

It acts like sodium chromoglycate but has antihistaminic properties which limits its use as an antiasthmatic.



**Table 3.58:** Drugs and their dosages

Drugs	Dose	Comment
• Hydrocortisone	Adult: In acute asthma or status asthmaticus IV hydrocortisone 200 mg after every 6 hours followed by oral prednisolone 40-60 mg daily for 2 weeks in tapering dose	• It is used in conjunction with other therapy to acute severe asthma
• Prednisolone	Oral 30-40 mg given once daily in acute asthma, then it is tapered slowly by 5-10 mg every 5-7 days. Sudden withdrawal or rapid tapering of steroids result in frequent recurrence	• Its effect is not immediate, hence, it must be used with bronchodilators to achieve rapid and vigorous bronchodilation
• Beclamethasone	Inhalor 400 mcg in 2-4 divided doses daily Severe cases 600-800 mcg initially and then reduce the dose according to response Children 6-12 years: 50-100 mcg 3-4 times a day Rotahaler 200 mcg inhaled in rotahaler 3-4 times a day Children: 100 mcg 2-4 times a day	• Only for patients who require chronic treatment with corticosteroids for control of symptoms of bronchial asthma
• Budesonide	Inhalation: Adults—100 mcg/per metered dose; 1-2 puffs twice a day Children—1 puff bid	• Useful adjunct for control of asthma alone or with $\beta_2$ -stimulant
• Fluticasone	Inhalation 25-125 mcg/per metered dose Adults—100-1000 mcg twice daily Children—between 4 and 12 yrs: half the dose < 4 yrs not recommended	• Useful for control of acute asthma

**Table 3.59:** Mast cell stabilisers—sodium chromoglycate

Drug	Dosage	Comment
Sodium chromoglycate (5 mg/metered dose)	Inhalor: Adult and children 2 puffs 3-4 times a day	<ul style="list-style-type: none"> <li>• Avoid sudden discontinuation of therapy if used with steroids concurrently</li> <li>• Side effect—cough and throat irritation</li> </ul>

**Table 3.60:** Ketotifen

Drug	Dose	Comments
Ketotifen	Adults 1-2 mg twice a day orally with food Children over 2 yrs as 1 mg twice a day with food Not recommended for children below 2 yrs	<ul style="list-style-type: none"> <li>• Avoid its use during pregnancy and lactation</li> <li>• Slow withdrawal over a period of 2-4 weeks</li> <li>• Side effects—Drowsiness, dizziness, dry mouth impaired reactions (not to drive vehicle while on drug), occasionally CNS stimulation, weight gain</li> </ul>

**Uses**

- Prophylaxis of bronchial asthma similar to sodium chromoglycate.

**Doses** See the Table 3.60.

### Leukotriene Receptor Antagonists (Montelukast and Zonfirlukast)

They are selective CysLT<sub>1</sub> receptors antagonists that bind with high affinity to the receptors sites, prevent the

inflammatory mediators (leukotrienes) to exert their effect. By this mechanism, they reduce the early and late phase of the asthma. They are useful in mild to moderate asthma not controlled by steroids and  $\beta$ -agonists.

Montelukast is used orally as 10 mg at bed time. In children (4-14 yrs) dose is half.

Side effects include, abdominal pain, fever, dry mouth, insomnia, arthralgia, paraesthesias, nightmares.

# 4

# Radiology

## X-RAY CHEST

A chest X-ray is the common noninvasive investigation that helps not only in the diagnosis of respiratory disease but also in cardiovascular disease too, hence, should be performed routinely in these disorders.

An anteroposterior (AP view) X-ray chest is normally taken in emergency conditions mostly at the bed side; while the other view is posteroanterior (PA view) which is common in use in routine cases. These views in fact reflect the direction of the rays from the source to the plate. In PA view, the beam of rays falls from behind the patient and the heart size appears more or less normal; while in AP view the beam of rays falls from the front and the heart shadow appears as apparently enlarged.

The X-ray chest is read with respect to the following points;

### 1. View

Whether it is PA view or AP view.

### 2. Centralisation or Centering

Look at the clavicles, if they are at the same level, then X-ray is centralised; and if not then it is poorly centralised.

### 3. Penetration/exposure

If the bony cage, ribs and vertebral bodies are just visible through the cardiac shadow, then penetration is good. If they are too clearly visible, then it is over-penetrated and if not visible, then it is under penetrated (under exposed). In over-penetrated X-rays you are likely to miss low density lesions.

### 4. Sex

If breast shadows are visible, then X-ray belongs to the female patient.

### 5. Position of Diaphragm

The right dome of diaphragm is slightly higher than left due to presence of liver on the right. Both the costophrenic and cardiophrenic angles are clear.

### 6. Position of the Trachea

This is seen as a dark column representing the air within the trachea. Note whether trachea is central or displaced. This is seen in reference to central bony vertebral column behind it. The trachea may be deviated to the same side or opposite side in a number of conditions (Read the deviation of trachea in clinical methods).

### 7. Bony Cage

Note the central vertebral column and the horizontal ribs. Decide whether chest is symmetrical or any scoliosis present. Examine whether the ribs are unduly crowded (collapse or fibrosis) or widely separated (pleural effusion, pneumothorax) on one side than the other. Look for any cervical rib, bony erosion of the ribs.

### 8. Degree of Inspiration

To judge the degree of inspiration, count the number of ribs above the diaphragm. The anterior end of the 6th rib should be above the diaphragm as should be the posterior end of 10th rib. If more ribs are visible then the lung is hyperinflated. If fewer ribs are visible, then patient

has not held the breath during full inspiration. It is important to note this because poor inspiration will make the heart size to look larger and cause the trachea to appear deviated to right.

## 9. The Cardiac Shadow

It occupies the central part of the chest. Its right and left borders are defined;

- i. The right border is smooth, formed from above downwards by the superior vena cava, right atrium and inferior vena cava.
- ii. The left border is formed from above downwards by aortic knuckle, pulmonary conus (artery), left atrial appendage, and left ventricle.
- iii. The cardiothoracic ratio is <50 per cent i.e. the heart shadow is less than half of the maximum transthoracic diameter. If the cardiac shadow occupies >50 per cent of the transthoracic diameter, then heart is said to be enlarged.

## ABNORMALITIES ON CHEST X-RAY (PA AND AP VIEWS)

### Abnormalities of the Cardiac Shadow

*Causes of prominent aortic knuckle*

- Aortitis
- Aortic aneurysm
- Atherosclerosis of the aorta
- Post-stenotic dilatation.

*Pulmonary conus is prominent in;*

- Idiopathic dilatation of pulmonary artery
- Post-stenotic dilatation
- Pulmonary hypertension

*The pulmonary artery shadow* It is absent in pulmonary valvular stenosis, pulmonary artery atresia, Fallot's tetralogy

*Left atrial enlargement* It produces double atrial shadow and prominence of shadow of left atrial appendage and straightening of the left border. It is seen in mitralised heart. The right atrial enlargement produces straightening of the right border of the heart with double atrial shadow.

*Ventricular enlargement* It produces enlargement of cardiac shadow in different directions. The right ventri-

cular enlargement produces enlargement of cardiac shadow outwards; while left ventricular enlargement causes the heart shadow to enlarge down and out giving an appearance of *boot-shaped heart*.

## The Lung Fields

For radiological purposes, the lung fields are divided into three zones. The **upper zone** extends from the apex to a transverse line drawn through the lower borders of the anterior ends of the 2nd costal cartilages. The **mid-zone** extends from this line to another line drawn through the lower borders of the 4th costal cartilage. The **lower zone** extends from this second line to the bases of the lungs or to the dome of diaphragm. Each zone is examined on both sides and compared with each other for any abnormal finding.

### Chest X-ray (Lateral View)

This view is most useful in localising the lung lesion because interlobar fissures are clearly seen in this view. It should be examined in a systematic manner i.e.

- Bony cage
- Position of trachea
- The diaphragm (as the level of the domes of diaphragm differs on the two sides, a double shadow may be seen).
- The lung fields. The lung fields are obscured by two relatively opaque shadows one above and behind due to shoulder joint and second below and in front due to the heart.

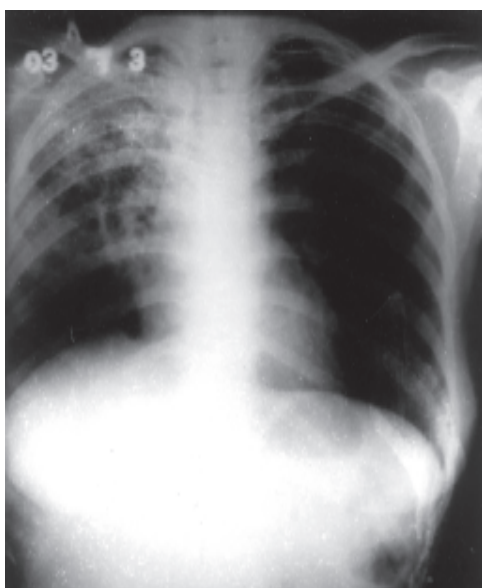
The abnormality on lateral view is detected by distortion of interlobar fissures which are seen as lines. The shrinkage of a lobe from collapse or fibrosis distorts these fissures/lines.

### The Hilum

Look at the hilum. The left hilum is higher than the right though the difference is usually <2.5 cm. Compare the shape and density of the hila. They are concave in shape and look similar to each other.

## CHEST X-RAY IN PULMONARY DISORDERS

Certain patterns encountered on chest X-ray in pulmonary diseases are;



**Fig. 4.1:** Apical tuberculosis. There is infiltration in right upper zone without cavitation



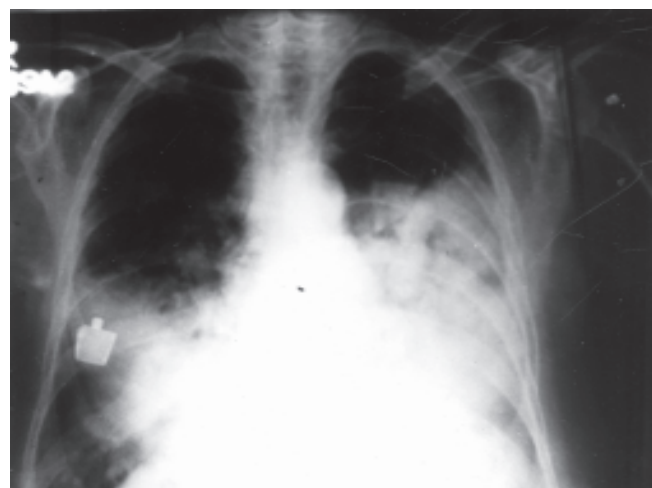
**Fig. 4.2:** Consolidation right middle lobe (chest X-ray PA view)

### Infiltrate

It is an abnormal shadow in the lung which does not have any pattern—a vague term (Fig. 4.1). If these infiltrates involve the alveoli such as in pneumonia and lymphoma, a homogeneous dense opacity is produced. When this opacity is confined to a lobe, it is called *lobar consolidation* and this is seen in bacterial pneumonia (Figs 4.2 and 4.3). An air bronchogram is also seen. Multiple such opacities when present in the lung constitute bronchopneumonia. The alveolar exudates may coalesce to produce nodular opacities (Fig. 4.4) or large fluffy cottonwool like shadows (Fig. 4.5).

Alveolar infiltrates are patchy, homogeneous and have an air bronchogram. They may be lobar or segmental

Contrary to this, interstitial infiltrates occur when there is involvement of interstitium as in viral pneumonias, interstitial pneumonitis and occupational disorders. The radiological patterns that arise from these infiltrates reflect as micronodular, reticular, reticulonodular and multiple linear shadows. On occasion both alveolar and interstitial infiltrates get superimposed on each other such as occur in pulmonary oedema.



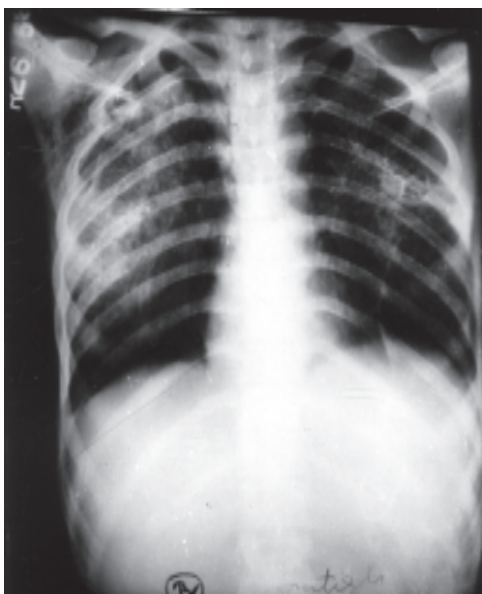
**Fig. 4.3:** Bilateral consolidation of lower lobes

## THE WHITENESS (OPACIFICATION) OF THE LUNGS

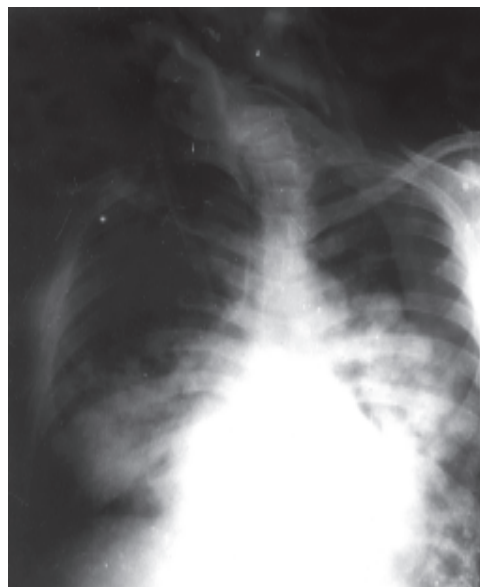
### Acute Pulmonary Oedema

In pulmonary oedema, there is leakage of fluid from the pulmonary venous circulation into the alveoli and the lung interstitium producing haziness of the lungs from the centre towards the periphery on both the sides. Acute pulmonary oedema may be cardiogenic (heart size is





**Fig. 4.4:** Bilateral pulmonary tuberculosis. Note the bilateral infiltrates producing nodular opacities



**Fig. 4.6:** Cardiogenic pulmonary oedema. Chest X-ray (PA view) shows bilateral haze extending from the centre to the periphery. There is enlargement of heart shadow



**Fig. 4.5:** Bilateral fungal infection. Note the fluffy cotton-wool shadows

enlarged due to left heart failure) or noncardiogenic (ARDS- type I respiratory failure) in which there is opacification of peripheral fields of the lung with normal cardiac size.

#### Radiological Findings

Radiological findings in the cardiogenic pulmonary oedema (Fig. 4.6) are;

1. *Haziness of the lung.* Severe pulmonary oedema due to LVF gives confluent alveolar shadowing (haziness) which spreads from the hilum towards periphery giving a “bat’s wing appearance”. In ARDS, the haziness is more peripheral than central.
2. *Upper lobe veins prominent.* In PA view in erect position, normal blood flow is greater in the lower lobes than the upper due to gravity, hence lower blood vessels are more prominent. In heart failure (pulmonary oedema), the upper lobe veins are dilated due to diversion of blood flow – the first sign of the heart failure.
3. *Size of the heart.* Heart size is enlarged.
4. *Kerley’s B lines.* These are caused by oedema of the interlobular septa. They are horizontal, nonbranching white lines best seen at the periphery of the lungs just above the costophrenic angle.
5. *Pleural effusion or hydrothorax.* A small pleural effusion obliterating the costophrenic angle is common.



### Differential Diagnosis of Pulmonary Oedema (Bilateral Haze in the Lungs)

Two common causes of pulmonary oedema (*cardiogenic* vs *noncardiogenic*) are compared in the Table 4.1.

**Table 4.1:** Radiological comparison of cardiogenic vs noncardiogenic pulmonary oedema

Features	Cardiogenic oedema (Fig. 4.6)	Noncardiogenic oedema (Fig. 4.7)
Distribution of haze	Bilateral haze is more central than peripheral	Bilateral haze is more peripheral than central
Heart size	Enlarged	Normal
Upper lobe veins	Dilated and enlarged	Normal
Kerley B lines	Far more common	Less common
Pleural effusion	Common	Less common

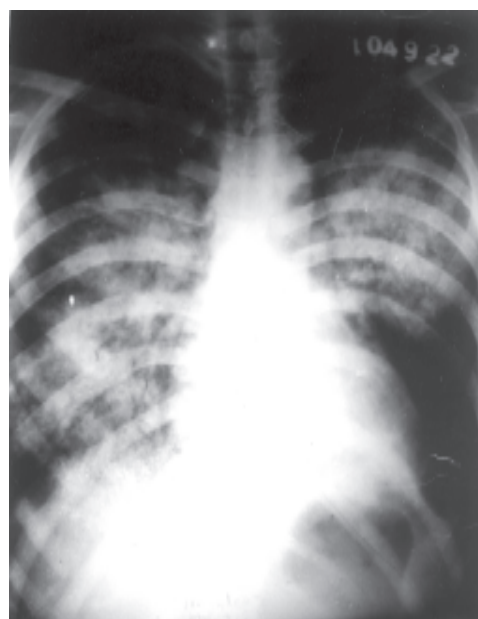
#### Causes of ARDS (Noncardiogenic pulmonary oedema)

ARDS is caused by any acute insult to either the alveolar or endothelial cells that result in loss of integrity of the junctions between these cells allowing fluid to leak into the alveoli. Causes include;

- Aspiration or inhalation of toxic gases
- Pneumonia
- Sepsis
- Drowning
- Hypersensitivity reaction
- Lung trauma
- Radiation
- Fat embolism (crush injury)
- Drug abuse
- Transfusion reaction

### Pulmonary Embolism

It produces a wedge-shaped or triangular opacity situated in one of the periphery in a patient suffering from deep vein thrombosis (Fig. 4.8). The dome of the diaphragm may be raised on that side. It may lead to a small pleural effusion. There may be collapse or linear atelectasis. Pulmonary embolus can also lead to black area of underperfused lung which is difficult to detect on plain X-ray. CT scan and MRI are diagnostic. The enlargement



**Fig. 4.7:** Noncardiogenic pulmonary oedema. Note the peripheral haze and normal cardiac shadow

of heart and prominent pulmonary conus suggests acute cor pulmonale.

### Homogeneous Opacity Involving One Hemithorax

The causes are:

- Pleural effusion



**Fig. 4.8:** Pulmonary embolism. There is an peripheral opacity (arrow) in the right lung. The pulmonary conus is prominent and heart shadow is not enlarged, probably due to emphysema

- Consolidation
- Atelectasis
- Pulmonary agenesis
- Pneumonectomy.

Ipsilateral shift of the trachea and mediastinum, narrowing of the intercostal spaces, elevation of dome of diaphragm and compensatory emphysema of the uninvolved side indicate *atelectasis*, or collapse, fibrosis *pneumonectomy* and *pulmonary agenesis*. The collapse and fibrosis of the lung have been dealt separately.

The contralateral shift of the trachea and mediastinum, the homogeneous opacification in the peripheral lung field with concave border towards the lung, widening of the intercostal spaces, obliteration of costophrenic angle and nonvisibility of the dome of diaphragm on the involved side indicate pleural effusion (Figs 4.9A and B).

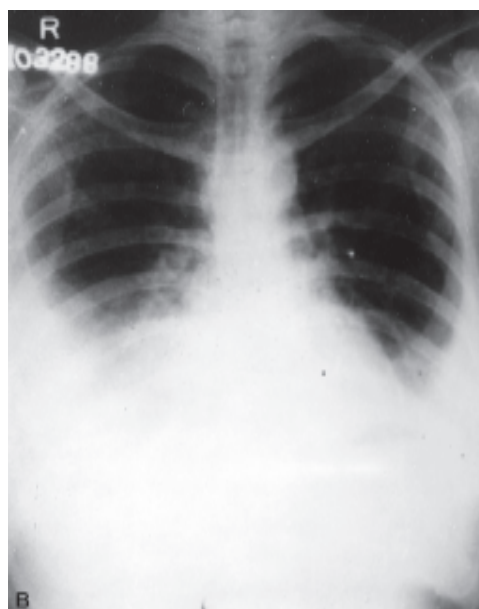
In mild pleural effusion, there may be just obliteration of costophrenic angle (Fig. 4.10); while a localised effusion produces a homogeneous opacification similar to a tumour with no shift of trachea or mediastinum (Fig. 4.11).

In massive consolidation, a rim of normal lung tissue at costophrenic angle may be seen. There may be no shift of trachea or mediastinum. No compensatory emphysema is seen.

### A Lobar Homogeneous Opacity

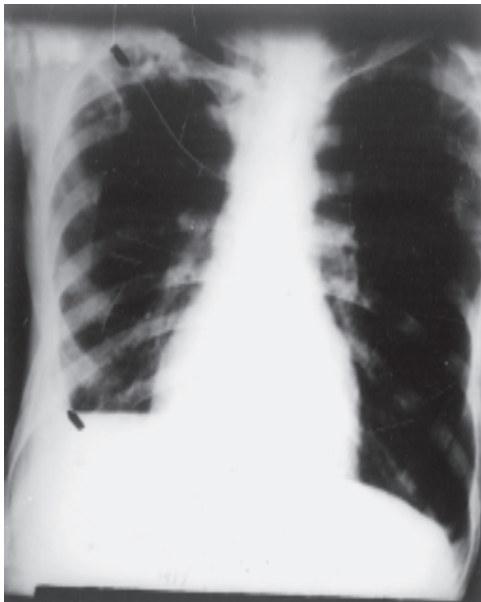
A homogeneous opacity look like an area of white lung. If there is a patch of opacity, it could be due to collapse, pleural effusion or consolidation. If the opacity is uniform with a well demarcated border, then it is either a lobar collapse or pleural effusion which can be differentiated by shift of the trachea and mediastinum with crowding of the ribs and elevated dome of the diaphragm on the side involved in case of collapse but reverse will happen in pleural effusion (shift of trachea and mediastinum to opposite side, widening of the intercostal spaces and flattening of the dome of diaphragm). If the shadow is not uniform and the border is not well defined then it could be either consolidation or fibrosis. In fibrosis, the signs are similar to collapse of the lung. In consolidation (Fig. 4.12), note the followings;

- Presence of air-bronchogram within opacity (arrow) confirms the diagnosis of consolidation. In

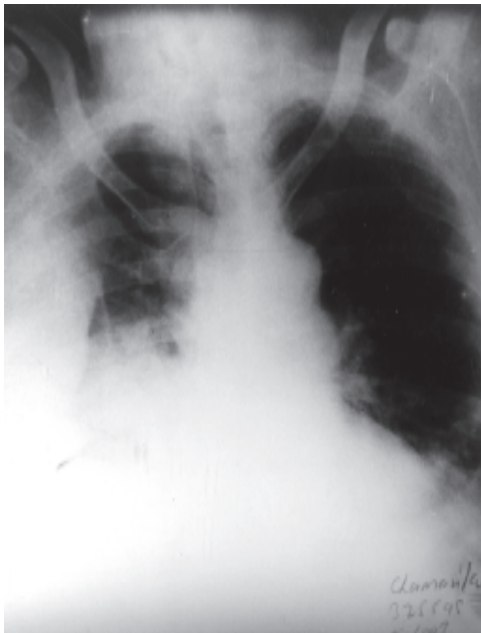


**Figs 4.9A and B:** A. Homogeneous opacity of one hemithorax. Chest X-ray PA view showing pleural effusion, B. Bilateral pleural effusion. There is bilateral opacification of thorax besides the heart. There is no deviation of trachea or mediastinum

consolidation, the air spaces are filled with fluid or exudate making them appear as white whereas airways within opacity retain air, making them appear black. The areas of blackness within white background suggest air-bronchogram.

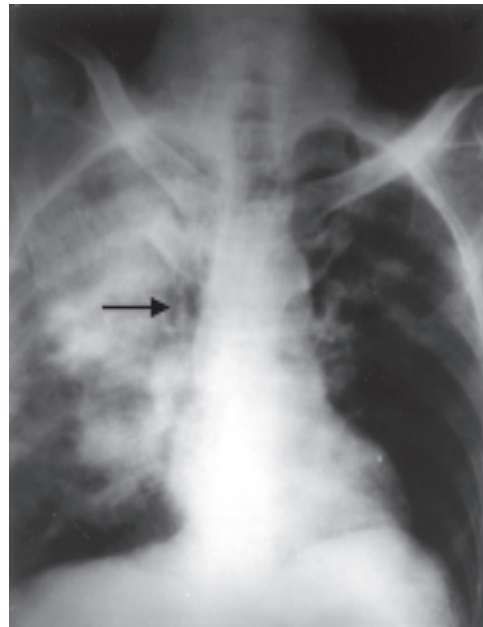


**Fig. 4.10:** Minimal pleural effusion. There is just obliteration of costophrenic angle (↑)



**Fig. 4.11:** Loculated pleural effusion. There is lobulated homogeneous opacity with no shift of trachea or mediastinum

- The shadowing in consolidation gets denser as one moves down the lung because fluid sinks and makes the lower border denser and well defined.

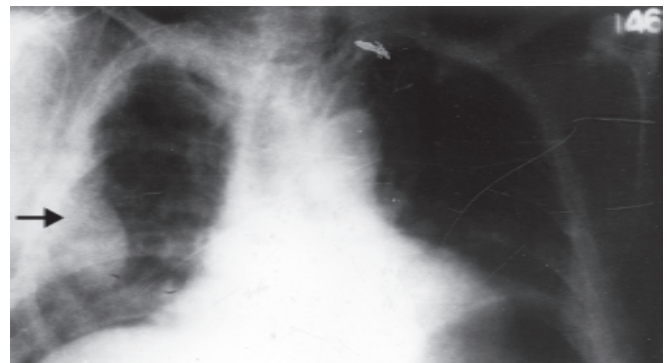


**Fig. 4.12:** Chest X-ray (PA view) showing consolidation of the right upper and middle lobe

### Coin-shaped Shadow

The term *coin lesion* is used to describe an area of whiteness situated within a lung field (Fig. 4.13). It needs not be strictly circular. The causes of single coin lesion are:

- Benign tumour e.g. haematoma
- Malignant tumour e.g. bronchial carcinoma, solitary secondary
- Infection e.g. consolidation, abscess, tuberculosis (tuberculoma)
- Hydatid cyst



**Fig. 4.13:** Chest X-ray (PA view) showing a coin shaped lesion (arrow). The lesion is single and larger than a coin

- Pulmonary infarction
- Rheumatoid nodule.

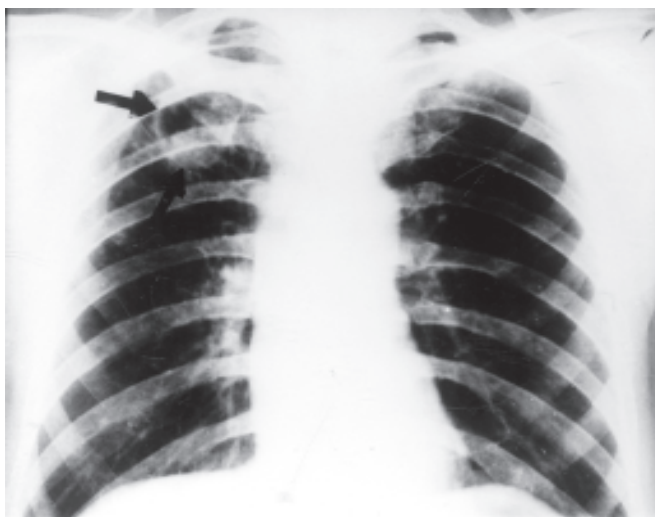
#### Differentiating Features

- A speckled irregular or lobulated edge of the lesion suggests malignancy
- Calcification within the lesion indicates tuberculosis or infection
- More than one coin shaped lesions suggest metastatic disease
- Air bronchogram suggests consolidation rather than a tumour
- Surrounding the lesion, the area of consolidation or collapse may indicate a tumour
- Malignant tumours are associated with mediastinal lymphadenopathy, rib erosion and pleural effusion.

#### Cavitary Lung Lesion

A cavity is a walled off area of the lung which is darker in the centre than the periphery (Fig. 4.14). Some coin-shaped lesions may cavitate. The causes of cavitating lung lesions are:

- Lung abscess (e.g. tubercular, pyogenic, malignant)
- Neoplasm with secondary degeneration and cavitation
- Cavitation around a pneumonia



**Fig. 4.14:** An opical tubercular cavity

- An infarct (rare)
- Rheumatoid nodule (rare)

#### Differential Features

- The cavity may contain a horizontal fluid level – a line within lesion. There will be whiteness (fluid) below the line with an area of blackness (air) above. This is common in pyogenic infection, i.e. lung abscess (Fig. 4.15A).
- If the walls of the cavity are thick (>5 mm) and irregular, infiltrating into the surrounding lung, then it is a neoplasm as opposed to an abscess. Staphylococcal abscess especially is a thin-walled called *pneumatocoele*. This rule does not always hold true.
- A white ball within a cavity is characteristic of an aspergilloma which can be seen floating in the cavity (Fig. 4.15B).

#### Ring Shadows (e.g. Bronchiectasis)

Multiple ring shadows of any size upto 1 cm in diameter occurring in groups giving a honey-comb or “bunches of grapes” appearance on chest X-ray may suggest bronchiectasis (Fig. 4.16). Other lesions described in bronchiectasis are;

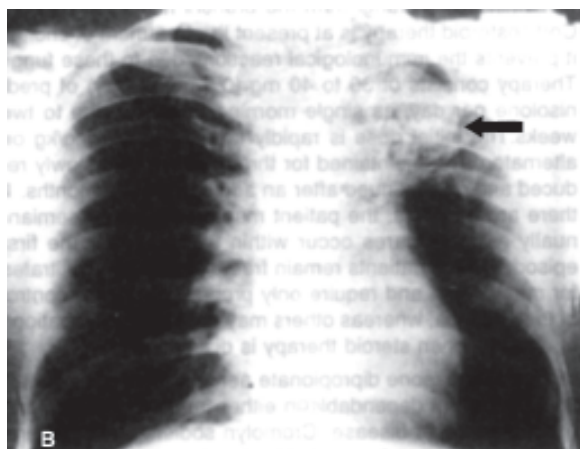
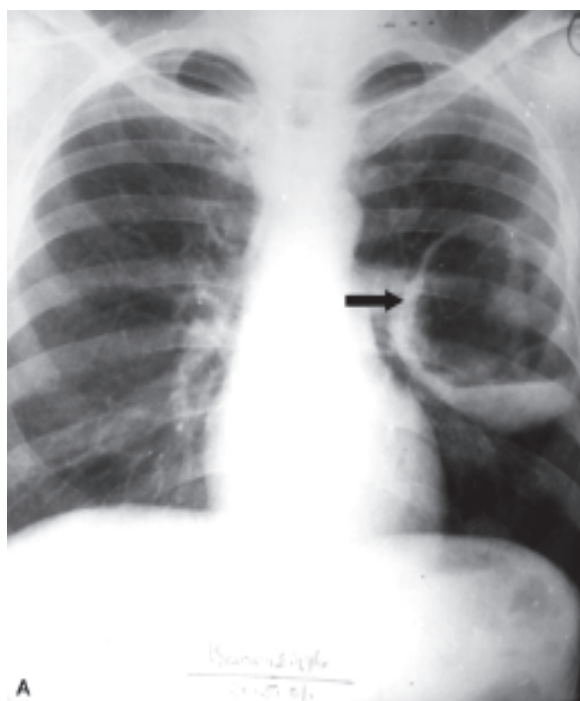
- *Tubular shadows*. These are thick white shadows upto 8 mm wide, represent bronchi filled with secretions (end-on bronchus).
- *Glove finger shadows*. These represent a group of tubular shadows seen head on and look like the finger of a glove.

The presence of any of these features suggests bronchiectasis but a normal chest X-ray does not however exclude the diagnosis. The CT scan is most sensitive diagnostic test available for bronchiectasis.

#### Causes of Bronchiectasis

1. *Structural* e.g. Kartagener syndrome, obstruction (foreign body, a growth)
2. *Infection* e.g. childhood pertussis or measles, tuberculosis, pneumonia
3. *Immune* e.g. hypogammaglobulinaemia, allergic bronchopulmonary aspergillosis



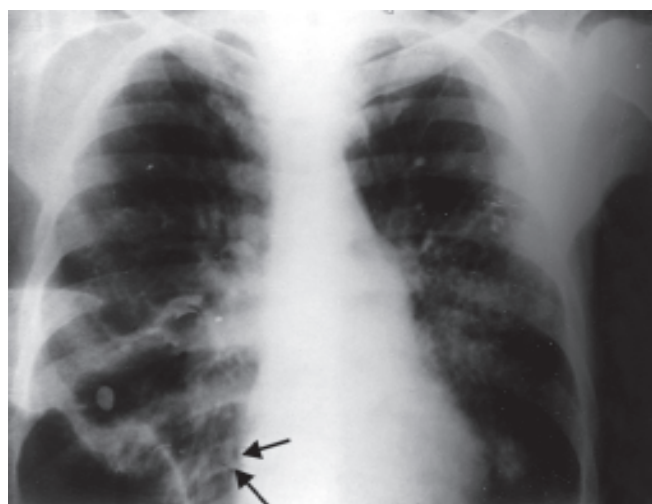


**Figs 4.15A and B:** Chest X-ray PA view: A. A lung abscess in left lung (arrow); B. A cavity with fungal ball in left upper zone (←)

4. *Metabolic* e.g. cystic fibrosis
5. *Idiopathic* e.g. secondary to stasis.

### Reticulonodular Shadows (Fibrosis or Oedema of the Lungs)

The reticulonodular shadowing which simply means a meshwork of lines that combines to form nodules and ring shadows of <5 mm in diameter. Sometime this



**Fig. 4.16:** Chest X-ray (PA view) showing multiple ring shadows suggesting bronchiectasis (←) of right lower lobe. In addition there is superadded infection due to aspiration pneumonia

meshwork is very fine giving a ground glass appearance, said to look like a thin veil over the lung. Later it gives a more coarse appearance and is said to look like a honey-comb. Honey-combing is a feature of interstitial lung disease/pulmonary fibrosis. The causes of reticulonodular opacities are;

- Pulmonary oedema
- Bronchopneumonia
- Lymphangitis carcinomatosa (Fig. 4.17).

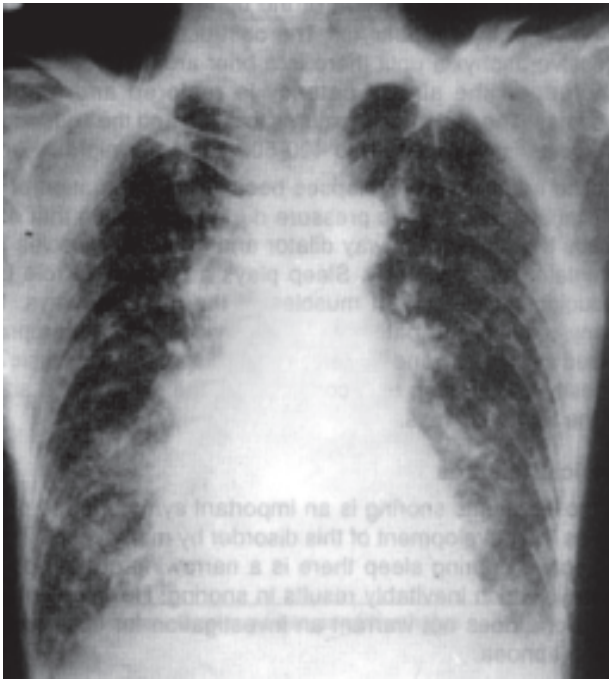
### Differentiating Features

- Bilateral basal reticulonodular shadowing could be either due to oedema or fibrosis. Shadowing that is confined to midzone or apical region is more likely to be fibrosis
- The presence of small lungs indicates fibrosis rather than pulmonary/ interstitial oedema
- Shifting of the mediastinum to the side of shadowing is due to fibrosis rather than oedema
- In fibrosis, heart border and diaphragm on the side involved appear blurred
- Vascular marking is less distinct in area of fibrosis.

### Causes of Fibrosis

- Cryptogenic





**Fig. 4.17:** X-ray chest showing lymphangitis carcinomatosa

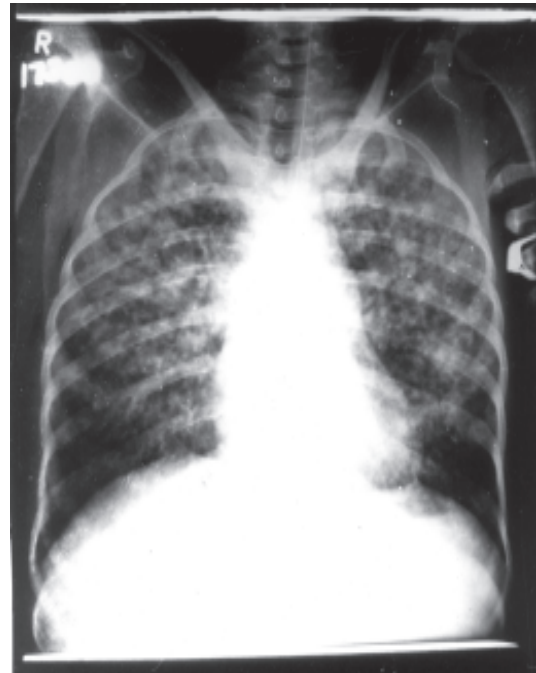
- Occupational lung disease e.g. extrinsic allergic alveolitis, asbestosis
- Infection e.g. tuberculosis, psittacosis, aspiration pneumonia
- Collagen vascular disorders e.g. rheumatoid arthritis, SLE
- Sarcoidosis
- Iatrogenic e.g. amiodarone, busulphan, radiotherapy.

### Miliary Shadowing

Miliary shadowing refers to small miliary opacities having similar density and size distributed in the lung(s) giving a spotted or mottled appearance. They sometimes can be confused with a ground glass appearance or normal vascular markings of the lung. To differentiate between them, move close to the X-ray and examine the shadowing carefully.

In miliary mottling, the opacities are discrete, small and have similar size and density, are mainly distributed in the peripheral lung fields (Fig. 4.18). The main causes of miliary mottling are;

- Tuberculosis



**Fig. 4.18:** Chest X-ray (PA view) showing miliary mottling appearance due to miliary tuberculosis

- Sarcoidosis
- Disseminated metastases in the lungs
- Interstitial lung diseases.

### Differentiating Features

- *Distribution of opacities.* In miliary tuberculosis, the opacities are most marked in the upper zone, in sarcoidosis, these are most marked in perihilar region and mid-zones; while in miliary metastases these are limited to lower zones.
- *Density.* Highly dense white opacities are likely to be due to dust related industrial/occupational disorders or calcified tuberculosis. Less dense changes could either be multiple secondaries or sarcoidosis or any other cause of miliary mottling.
- *Other associated signs.* Unilateral hilar enlargement suggests tuberculosis while bilateral hilar enlargement (lymphadenopathy) indicates sarcoidosis. Presence of subtle cavitating lesions suggest tuberculosis.

### Collapse of the Lung

Collapse of the lung means an area of the lung devoid of air, hence, is detected as a white area within lung fields.

*Radiological Features (Fig. 4.19)*

1. *Lung fields.* Look at the lung fields. The right lung normally is larger than the left – if it is not, then suspect an area of right lung collapse.
2. *Position of diaphragm.* Normally, left dome should be lower than the right, if it is not (e.g. left dome elevated) then left lung collapse may be suspected.
3. *Position of the horizontal fissure.* Note the position of the horizontal fissure in the right lung. The horizontal fissure normally on the right should run from the centre of the hilum to the level of the 6th rib in the axillary line. If this is pulled up, it suggests right upper lobe collapse and if pulled down then right lower lobe collapse should be suspected.
4. *Position of the heart.* The heart shadow lies in the midline with one – third to the right and two – thirds to the left. The heart shadow gets deviated to the side of collapse.
5. *Heart borders.* Define the heart borders. Normally the borders are distinct. If the adjacent lung is collapsed, then the heart border will appear blurred. For example, if right heart border is blurred this indicates right middle lobe collapse; and if left is indistinct or blurred, then suspect lingular collapse.
6. *Position of trachea.* Normally trachea is central; it gets deviated if there is pathology in the upper lobes. Collapse of right or left upper lobe will pull the trachea towards the area of collapse (Figs 4.19A to D).

*Note.* To determine the collapse of the lung both PA view and lateral chest X-rays must be taken and examined

7. *Lateral films.* Check the position of oblique and horizontal fissures. The horizontal fissure appears as faint white line which should pass horizontally from the hilum to the anterior chest wall. If this line is not horizontal, the fissure is displaced. The oblique fissure should pass obliquely downwards from the T4/T5 vertebrae, through the hilum, ending at the anterior third of the diaphragm.

Collapse of any of the lobes of the lungs gives a distinct appearance on X-ray (Figs 4.20 and 4.21).

*Collapse of Whole Left Lung vs Pneumonectomy (Fig. 4.20)*

The distinct features are:

1. In pneumonectomy, the left hemithorax is homogeneously opaque with no lung markings while in collapse, lung markings are visible.
2. In pneumonectomy, the whole mediastinum and even a portion of right lung lies in left hemithorax while in collapse only mediastinum is shifted.

**Calcification in the Lung Fields***Causes**Parenchymal calcification***A. Diffuse**

- i. Infection e.g. tuberculosis, abscess, histoplasmosis, pneumonia
- ii. Tumours e.g. Haematomas, metastases
- iii. Unknown e.g. Alveolar microliths, broncholitis
- iv. Silicosis
- v. Haemosiderosis (following haemoptysis in mitral stenosis)

**B. Solitary**

- Tuberculosis
- Histoplasmosis
- Hamartomas (pop-corn calcification)

*Pleural calcification**Diffuse*

- Tuberculosis (Fig. 4.22), empyema
- Asbestosis

*Focal*

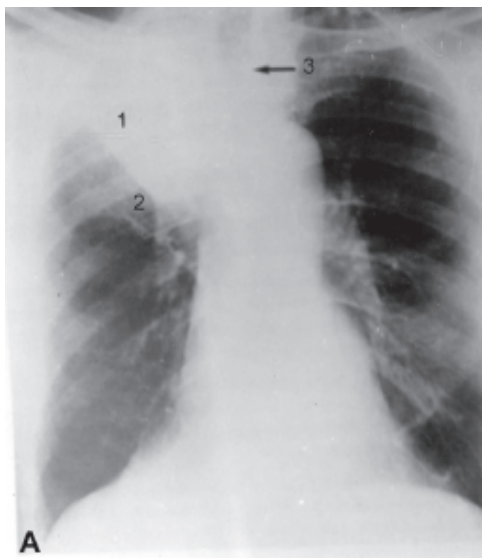
- Asbestosis (Fig. 4.23)
- Talcosis

*Egg-shell calcification (Fig. 4.24)*

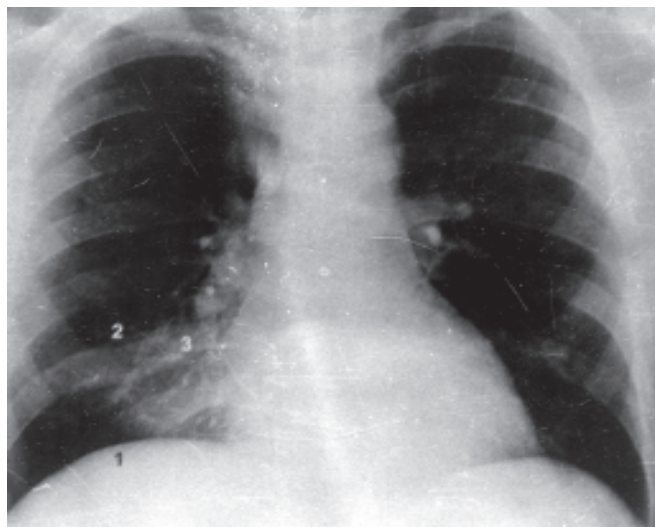
- Silicosis (commonest)
- Coal-miner's pneumoconiosis
- Sarcoidosis

*Mediastinal Calcification*

- Lymphadenopathy e.g. sarcoidosis, tuberculosis, pneumoconiosis
- Tumours e.g. teratoma, dermoid, thyroid adenoma.



**Figs 4.19A and B:** Collapse of right upper lobe: A. A chest X-ray (PA view) shows an area of opacification in the upper zone (1) of right lung. The horizontal fissure (2) is pulled upwards. There appears to be a large right upper hilar mass. The trachea (3) is shifted to right i.e. same side of the mass. The ribs over the area of opacification are crowded with narrowing of intercostal spaces, B. Chest X-ray (lateral view) shows the area of opacification localised to upper most portion of the lung

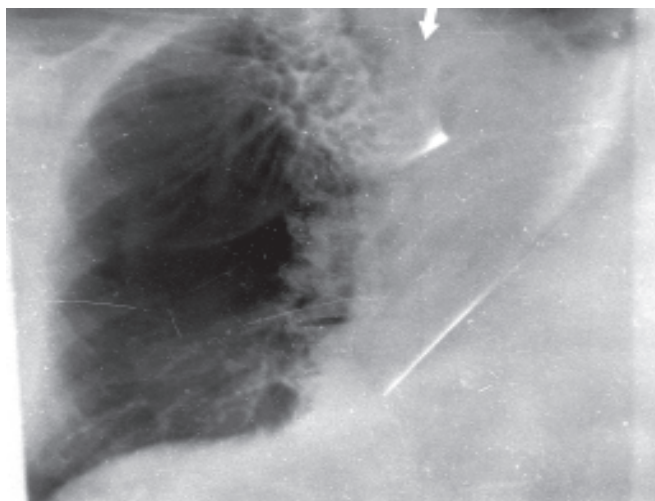


**Fig. 4.19C:** Collapse of right middle lobe. It is difficult to spot. The right diaphragm may be raised (1), and horizontal fissure may be lower than usual. The lower zone of right lung shows a haze (3) with indistinct heart border. It is easier to detect on lateral film (not projected) where a triangular opacity with its apex towards-hilum and its base running between sternum and diaphragm will be seen similar to collapse of left lower lobe (lingular collapse) in Fig. 4.19D



**Fig. 4.19D:** Left lower lobe (lingular) collapse. Chest X-ray lateral view shows a triangular opacity with apex towards hilum and base between sternum and diaphragm

**Figs 4.19A to D:** Collapse of different lobes of the lungs on chest X-rays (PA and lateral views)



**Fig. 4.20:** Pneumonectomy. Chest X-ray (PA view) shows that left hemithorax is white. The mediastinum lies in the left hemithorax and some of the right hypertrophied lung has herniated to the left side giving a slightly darker left apex (arrow) compared to base. This picture can be confused with collapse of left lung (whole)

#### Cardiac calcification

- Aortic arch (ring shaped or annular calcification in atherosclerosis)
- Pericardial calcification (adhesive or constrictive pericarditis)
- Calcification of mitral and aortic valves
- Thrombi and left atrial myxoma
- Calcification of coronary arteries

#### Chest wall Calcification

- Soft tissue e.g. cysticercosis, Guinea-worm
- Ribs (costal cartilage)
- Phleboliths

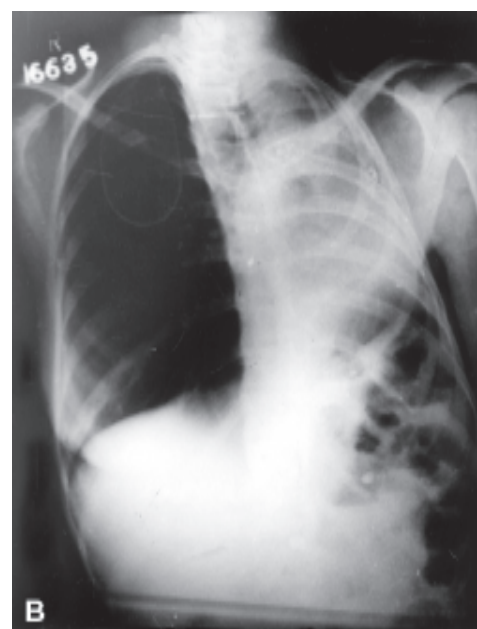
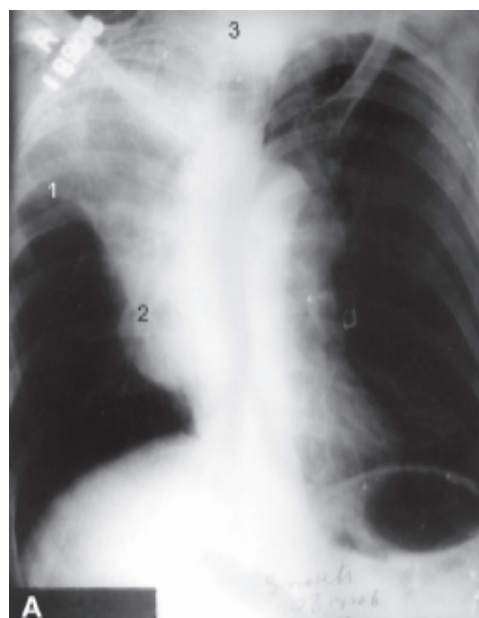
### THE BLACK ( HYPERTRANSLUCENT) LUNG FIELDS

#### Hypertranslucency

It refers to increased blackness of the lung fields due to trapping of air either in the pleural space or in the lungs. It may be unilateral or bilateral.

#### Caution

Before commenting on hypertranslucency, check the penetration of X-ray. If the vertebral bodies are just hardly visible behind the heart, it is a good quality X-ray while



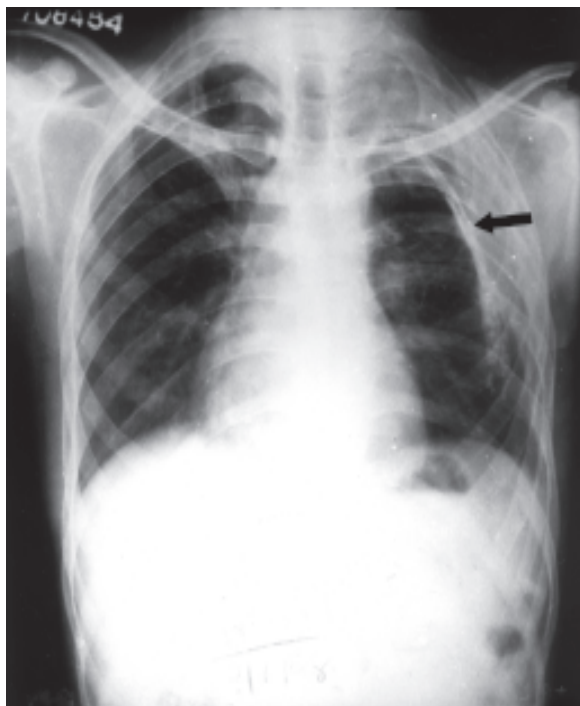
**Figs 4.21A and B:** Bronchogenic carcinoma.

Chest X-ray (PA) view shows;

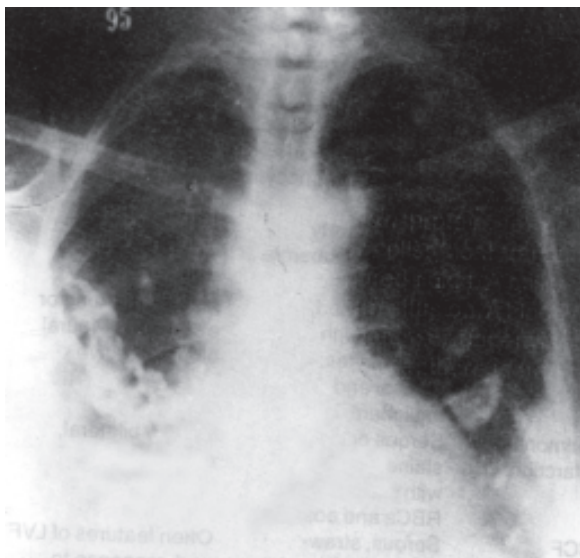
**A.** Collapse of right upper lobe. Note the area of whiteness in upper zone of right lung. The horizontal fissure is elevated (1); there is shift of mediastinum to right side (2). The trachea is deviated to the right (3). The ribs over the area of whiteness are crowded. On lateral film, the increased whiteness in the uppermost part of the chest will be seen (not depicted).

**B.** Left upper lobe collapse. When it collapses, it causes haze to appear over the whole of the lung as it occupies major portion of the lung field on PA view. On the lateral film, an area of whiteness will be seen on the top of left lung (not shown). There is deviation of trachea and heart shadow towards the collapsed lung. The ribs spaces are narrowed on left side



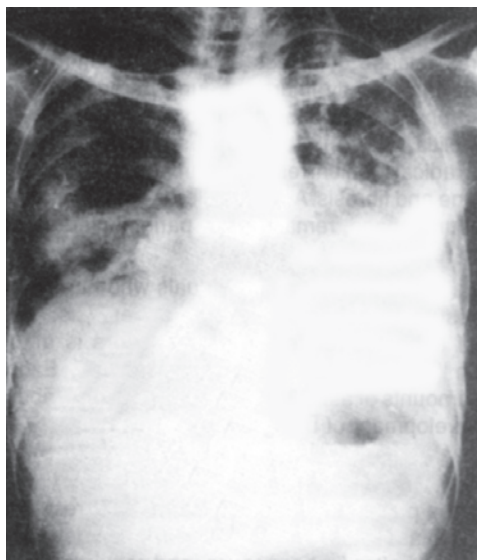


**Fig. 4.22:** Pleural calcification (diffuse) in tuberculosis on the left side of the lung (←)



**Fig. 4.23:** Asbestosis. Chest X-ray PA view shows bilateral opacities in the lower zones with pleural plaques of calcification

if they are clearly visible, then film is overpenetrated and makes the lungs appear black (hypertranslucent).



**Fig. 4.24:** Egg cell calcification. Chest X-ray (PA view) shows an egg cell calcification in hilar lymph nodes in silicosis

#### *Causes of Hypertranslucency*

##### *Unilateral*

- Pneumothorax
- Unilateral obstruction
- Bullae
- Eventration of the diaphragm

##### *Bilateral*

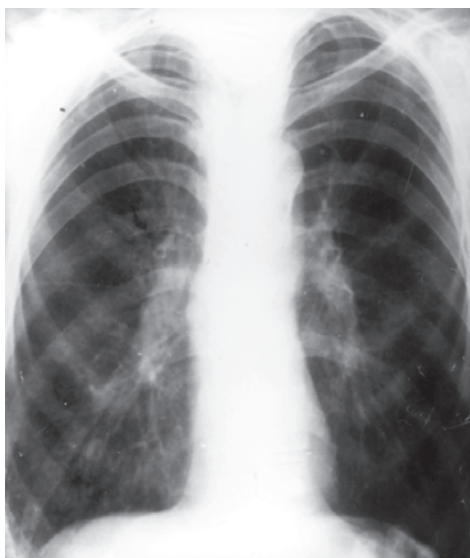
- Pneumothorax
- Bullous emphysema
- COPD
- Bronchial asthma
- Primary pulmonary hypertension (if vascular shadows disappear, the lung is replaced by air)
- Ebstein's anomaly
- Fallot's tetralogy

#### **Chronic Obstructive Pulmonary Disease (COPD)**

The radiological findings (Fig. 4.25) are due to hyperinflation of the lungs with constriction of the cardiac shadow.

- The lungs are large and voluminous due to hyperinflation which can be checked by counting the ribs anteriorly. If you can count more than 7 ribs above the diaphragm, then lungs are hyperinflated. This can be a normal finding in some individuals also.





**Fig. 4.25:** Chest X-ray showing COPD. Note all the characteristics described in the text

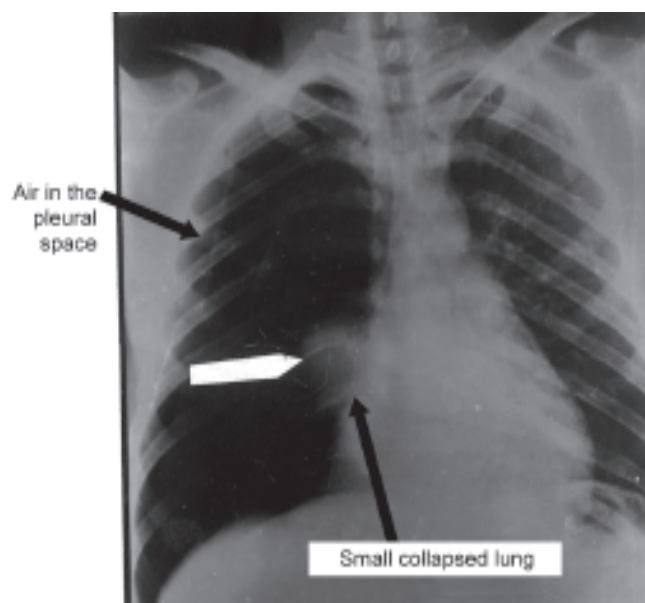
- The domes of the diaphragm are low and flat instead of being convex due to hyperexpansion of the lungs.
- The heart is tubular (elongated and narrow) due to overexpansion of both lungs. The heart, instead of sitting on the diaphragm often appears to “swing in the wind”
- Hypertranslucency of both the lungs is characteristic. Bullae (densely black areas of lung, usually round, surrounded by hairline shadows) may be seen which may compress the normal lung and distort the surrounding vasculature. Thus, to find out the bullae, look out for areas of decreased vascular markings.
- The lung vascular markings are reduced bilaterally (oligaemic lungs) and fan out as straight lines from the hilum but stop two-thirds of the way out i.e. peripheral pruning (peripheral fields appear without vascular markings).
- The ribs are more horizontal and the intercostal spaces appear widened.

### Pneumothorax (Unilateral Black Lung)

Before commenting on unilateral blackness, check the technical quality of film. A rotated film (one clavicle is nearer the midline than the other) may make one side less dense than the other.

### Radiological Features of Pneumothorax

- There is hypertranslucency of the lung in the periphery without vascular markings. This is due to air trapped in pleural space.
- There is sharply defined edge of the deflated lung, seen as a vertical line when X-ray is turned on its side which is convex towards periphery. In a large pneumothorax, deflated lung appears small towards the centre with convex borders (Fig. 4.26).
- The mediastinum is shifted away from the black lung indicating tension pneumothorax (Fig. 4.26) which returns to normal after removal of air and expansion of lung (Fig. 4.27).
- Differentiation between a bullae and pneumothorax is sometimes difficult and often impossible. However, if lung markings are seen either crossing the area of blackness or are limited to the periphery of the blackness, then it is a bullae rather than pneumothorax. Bullae are usually multiple if bullous disease is suspected.



**Fig. 4.26:** Pneumothorax. Right sided tension pneumothorax. Chest X-ray (PA view) before compression shows;

- Right lung is blacker than left
- The lung is collapsed towards the hilum and its outline is demarcated by a thin pencil line indicated by a white arrow
- Mediastinum is shifted to left
- The black area of pneumothorax (→) is devoid of vascular marking



**Fig. 4.27:** After decompression by intercostal tube, the lung has expanded

#### *Causes of Pneumothorax*

- Spontaneous
- Iatrogenic/trauma e.g. subpleural bleb rupture, transbronchial biopsy, central venous line insertion, ventilator-induced.
- Obstructive lung disease e.g. asthma, COPD
- Infections e.g. pneumonia, tuberculosis
- Cystic fibrosis
- Connective tissue diseases e.g. Marfan's syndrome, Ehlers-Danlos syndrome.

**Hydropneumothorax** is the term that denotes a fluid level (a horizontal line) above which lies blackness of the lung without lung marking (pneumothorax) and below (Fig. 4.28) there is opacification due to fluid.

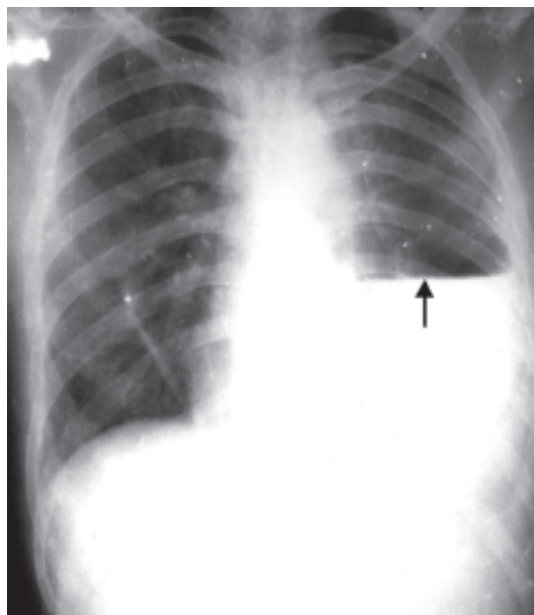
### **THE ABNORMALITIES OF SUBDIAPHRAGMATIC REGION AND THE DIAPHRAGM**

Finish your examination of chest X-ray by looking at the area under the diaphragm and the domes of diaphragm. The abnormalities in this area are;

1. Air under diaphragm
2. Elevation of diaphragm

#### **Air Under Diaphragm**

The area immediately under the diaphragm will usually be white due to presence of solid structures (liver and

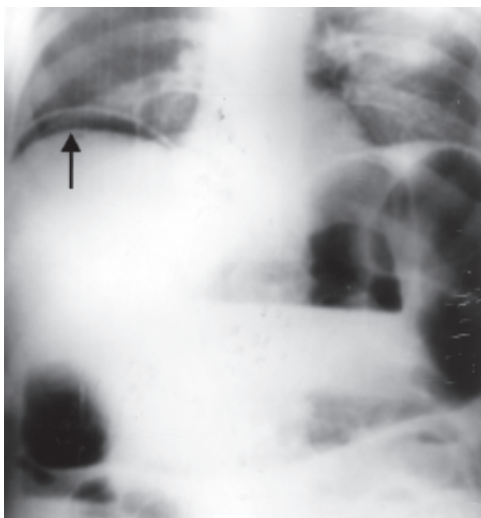


**Fig. 4.28:** Hydropneumothorax. Note the horizontal straight line (↑) between hypertranslucent area above and an opaque area below

spleen) except a darker round area under left diaphragm due to presence of air bubble in the stomach.

Air under the diaphragm is an important sign, since it indicates an intra-abdominal perforation (e.g. intestine, stomach, colon etc.). The air leaks from the intestines or stomach and collects under the diaphragm when X-ray is taken in standing position. The air under the right dome of diaphragm can easily be recognised as a rim of blackness (Fig. 4.29) immediately under the diaphragm (↑). However it is difficult to differentiate air under left dome from the normal stomach bubble as both produce blackness under diaphragm. The differences between the two are:

1. *Thickness of diaphragm.* The diaphragm appears as a thin white line between the white area below and the black lungs above. In the presence of air under left dome, this line becomes very thin ( $<5$  mm) as it consists of diaphragm only. Normally due to the presence of air bubble in the stomach, this line is thicker ( $>5$  mm) as it consists of diaphragm and the walls of the stomach.
2. *Length of air bubble.* Measure the length of air bubble. If it is longer than the half of the length of diaphragm, it is likely to be free air than stomach air bubble.



**Fig. 4.29:** Chest X-ray (PA view) showing air under right dome of diaphragm (indicated by an arrow). The X-ray was taken from a patient with enteric perforation. There is a large air bubble below the left dome

3. Look at the other dome i.e. right hemidiaphragm. If there is air bubble below the right and left hemidiaphragm (Fig. 4.29), it is likely to be free air in the abdomen.

### Elevation of Hemidiaphragm

The mid-point of right hemidiaphragm should be between the 5th and 7th ribs anteriorly ; while the left dome is lower than right by about 3 cm. The diaphragm placed above the 5th rib is said to be elevated which may be unilateral or bilateral.

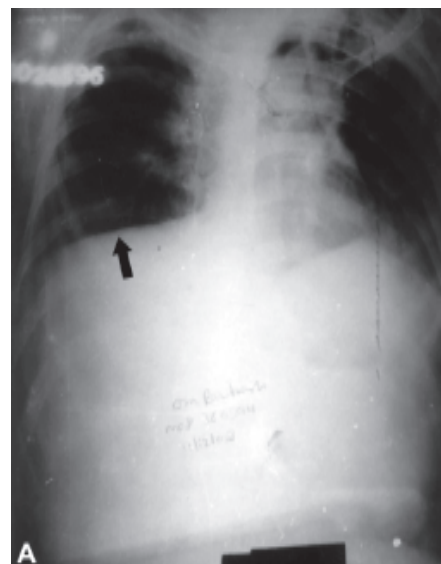
#### Causes

##### Unilateral elevation

- Subpulmonic pleural effusion (Fig. 4.30)
- Amoebic liver abscess
- Subdiaphragmatic abscess or a tumour
- Basal pulmonary infarction
- Basal pulmonary atelectasis/collapse
- Eventration of the diaphragm (Fig. 4.31)
- Phrenic nerve palsy
- Gas in the colon or fundus of the stomach

##### Bilateral elevation

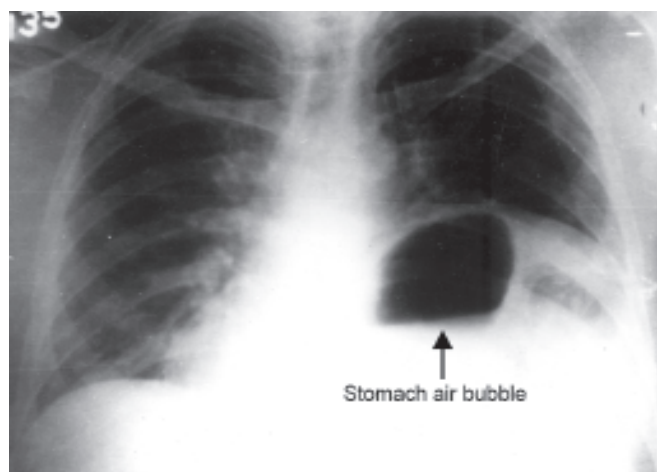
- Increased intra-abdominal pressure
- Pregnancy
- Obesity



**Figs 4.30A and B:** Subpulmonic pleural effusion: Chest X-ray (A) shows an abnormally elevated right dome of diaphragm with flattening (↑), gave a suspicion of diaphragmatic pleurisy or subpulmonic effusion, which revealed clearly a subpulmonic effusion (splash of fluid producing peripheral convex opacity with concavity toward lung) when chest X-ray (B) was taken in decubitus position

- Ascites
- Large abdominal masses
- Abdominal distension
- Infants
- Bilateral phrenic nerve palsy.

Clinically there is synchronous movements of the two hemidiaphragm. The paralysis of phrenic nerve is tested



**Fig. 4.31:** Chest X-ray (PA) view shows an elevated left hemidiaphragm due to eventration. Note the stomach air bubble in left hemithorax (↑), pushing the heart shadow to the right

by sniff test, i.e. while sniffing, the paralysed diaphragm under fluoroscopy will move paradoxically upward due to negative intrathoracic pressure.

### HILAR ENLARGEMENT (WIDENING OF HILUM)

Both the hila are similar in size and concave in shape. They have more or less same density. Abnormal hilum means either one hilum is bigger than the other or denser than the other. When hilum enlarges, its concave shape is lost – a first sign of hilar enlargement.

#### Causes of Hilar Enlargement

*Unilateral (Fig. 4.32)*

##### **Due to lymph node enlargement**

- Infective e.g. tuberculosis, histoplasmosis
- Sarcoidosis
- Neoplasm e.g. lymphoma, metastasis from bronchial carcinoma

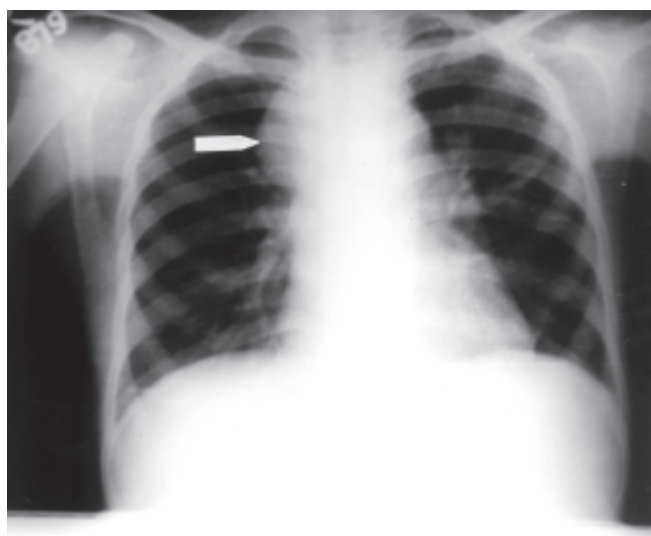
##### **Due to vascular enlargement**

- Pulmonary artery aneurysm
- Poststenotic dilatation of pulmonary artery

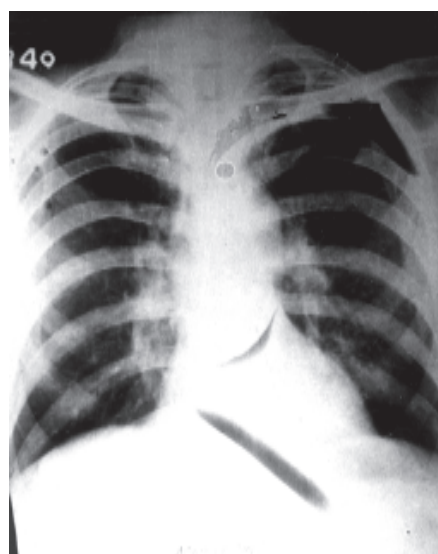
*Bilateral*

A. Bilateral lymph nodes enlargement (Fig. 4.33).

- Infections e.g. tuberculosis, histoplasmosis, AIDS, recurrent chest infections



**Fig. 4.32:** Chest X-ray (PA view) showing unilateral hilar enlargement due to lymphadenopathy (an arrow)



**Fig. 4.33:** Hilar enlargement. Chest X-ray (PA view) shows widening of the mediastinum due to bilateral hilar enlargement

- Neoplasms e.g. lymphoma, metastases
- Occupational lung diseases e.g. silicosis, berylliosis
- Sarcoidosis (a common cause)

#### Differential Features of Hilar Enlargement

1. Smooth enlargement of hilum is due to vascular lesion while lobulated appearance indicates lymphadenopathy and spiculated irregular or indistinct margins suggest malignancy.



2. Presence of calcification within the mass indicates lymph node enlargement usually tuberculosis. Egg shape calcification indicates lymphadenopathy due to silicosis.
3. Hilar enlargement due to malignant lung lesion is also associated with superior mediastinal lymphadenopathy
4. Look at the lung fields (for presence of tumour or tubercular infiltration) and bone/ribs for metastasis.

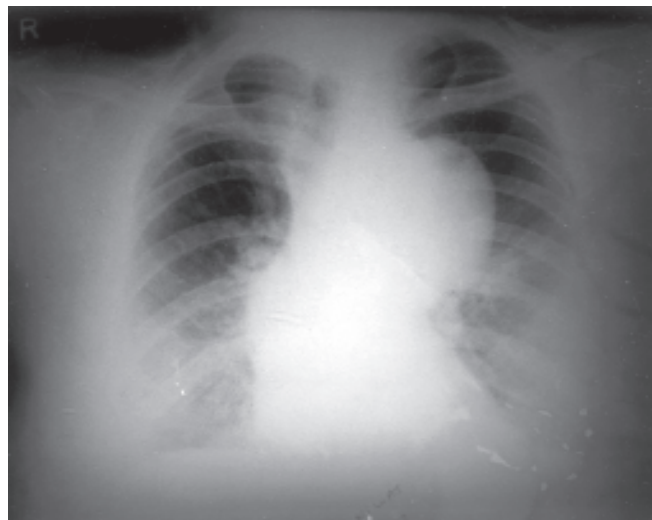
### Mediastinal Shadow/Enlargement

The mediastinum comprises the central area between the two lungs and their pleural coverings. Laterally on either side, it is bounded by mediastinal pleura. It extends from the thoracic inlet (above) to the diaphragm (below) and from the sternum (front) to the spine (back). The structures present in the mediastinum include, lymph nodes, heart and great vessels (aorta and its branches), superior vena cava, thymus, oesophagus and fatty areolar tissue.

N.B. On PA view, measure the width of mediastinum (white area) at its maximum convexity and compare it to the width of the chest at that point; if it is >30 per cent of the width of the chest, then mediastinum is said to be enlarged widened.

#### Causes of Mediastinal Widening (Enlargement)

1. *Lymphadenopathy*
  - Tuberculosis, sarcoidosis, lymphomas, leukemias, metastasis
2. *Aortic enlargement*
  - Aneurysm (Fig. 4.34)
  - Unfolding of aorta
3. *Thymus*
  - Thymoma
  - Thymic hyperplasia
4. *Cysts*
  - Dermoid; teratoma
  - Bronchogenic cyst
  - Pleuropericardial cyst
  - Meningocele
5. *Oesophagus*
  - Cardia achalasia



**Fig. 4.34:** Chest X-ray (PA view) showing widening of the mediastinum due to aortic arch aneurysm

- Hiatus hernia
  - Enterogenous cyst
6. *Miscellaneous*
- Lipoma
  - Mediastinal abscess
  - Ventricular aneurysm or cardiac tumour

#### Differentiating Radiological Features

1. *Site of enlargement/widening.* Look at the X-ray and note whether widening is at the top, in the middle or lower part of mediastinum.
  - Widening at the top could either be due to thyroid, thymus or innominate artery.
  - Widening of the middle or bottom of the mediastinum could be due to lymphadenopathy, aortic aneurysm, dilatation of oesophagus (cardia achalasia) or a hiatal hernia.
  - If widening is at the top, then look at the position of the trachea.

An enlarged thyroid will displace or narrow the trachea while tortuous innominate artery or thymus do not.

2. If you suspect an enlarged thyroid then look at the outline of the shadow.

• A thyroid has a well- defined shadow that tends to become less clear as one moves up to the neck.



3. Look at the right side of trachea. A white edge of trachea is 2-3 mm wide, its further widening suggest either enlarged superior vena cava or a paratracheal mass.
4. If you suspect widening of the aorta, follow the outer edge of the aorta downward, you may be able to detect a continuous edge which widens to form the edge of enlarged mediastinum. This would suggest that the widening is due to dilatation of the aorta.
5. Look at the calcification in the wall of aorta. If you detect a line of calcification then follow it. If it leads into an area of aortic knuckle, then this strongly suggests aortic aneurysm or atherosclerosis of aorta. If the line of calcification is separated from the edge of aortic shadow this strongly suggests aortic dissection.
6. To differentiate aortic aneurysm from unfolding of the aorta, follow both the edges of aorta and note for any widening which will suggest the aneurysm. Obtain a lateral film. If the edges of the aorta are parallel then you are probably dealing with unfolding of the aorta on the PA view of X-ray chest.

#### Surgical Emphysema (Fig. 4.35)

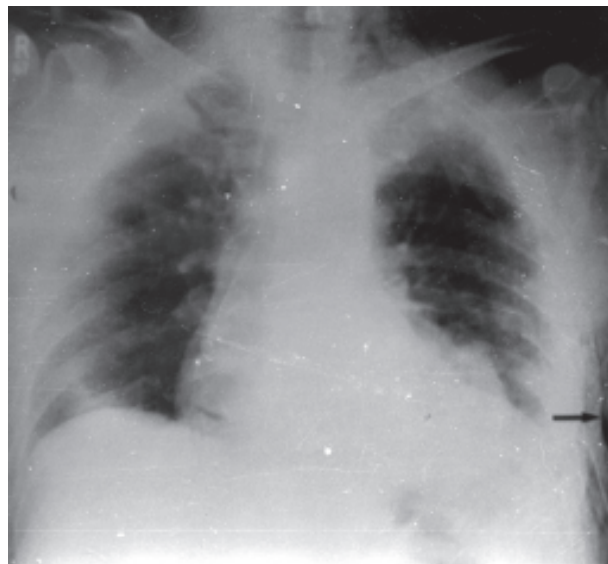
Collection of air in the soft tissue structure is called *surgical emphysema* because mostly it is due to either a complication of surgery or chest tube drainage.

##### Radiological Characteristics

- Look at the soft tissue shadow around the chest X-ray. Lozenge-shaped areas of blackness which represent pockets of air in the soft tissue indicate surgical emphysema (Fig. 4.35). These areas lie in the same plane as the soft tissue structures. In severe cases, orientation of the planes is lost and dark and white lines are produced which cross a part or whole of the film.

##### Causes of Surgical Emphysema

- Trauma
- Iatrogenic e.g. surgery, chest tube drainage
- COPD, asthma
- Oesophageal rupture
- Gas gangrene



**Fig. 4.35:** Chest X-ray (PA view) shows surgical emphysema. There is pocket of air outside the chest cage in the soft tissue indicated by an arrow (→) on left side

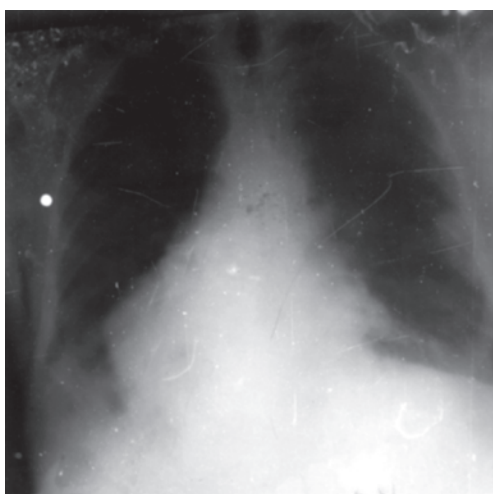
#### THE ABNORMAL HEART SHADOW

The major part of the heart shadow may lie on the right side than left, indicates either shift of the mediastinum to the right or mesocardium (heart lies in the centre) or dextrocardia (heart lies on the right-side instead of left).

##### Differential Radiological Features

1. First of all, always look for the radiographer marking, e.g. left or right at the top of X-ray. Incorrect marking can produce iatrogenic dextrocardia. If there is doubt, repeat the film
2. Look for the trachea. Shift of the mediastinum indicates shift of the heart due to collapse, fibrosis, pneumonectomy.
3. If marking is correct, and trachea is central, look at the apex of the heart, if it lies on the right, then it is dextrocardia (Fig. 4.36). Dextrocardia will be further confirmed by absence of aortic knuckle on the left side. It will be present on the right side.
4. Now look at the domes of diaphragm, higher left dome than right with air bubble below it confirms situs inversus.

The heart shadow is said to be enlarged if it occupies more than half of the transthoracic diameter.



**Fig. 4.36:** Dextrocardia. Note the followings

- (i) Apex of heart lies on the right side
- (ii) Aortic knuckle is absent on the left is present on the right side
- (iii) Left dome of the diaphragm is elevated due to presence of liver on left. There is absence of stomach air bubble below left dome

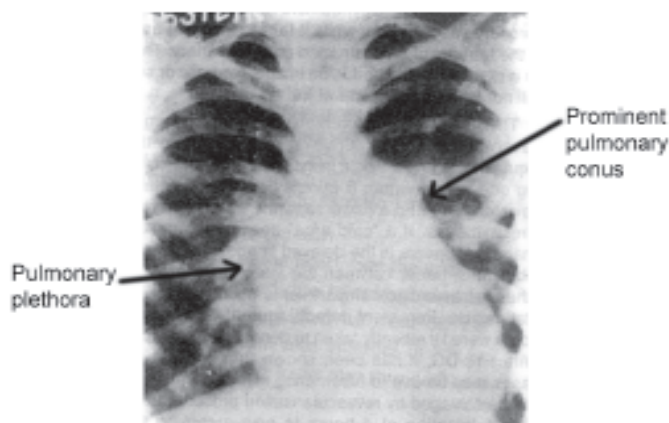
### Causes of Enlargement of Heart Shadow

1. Left to right shunt e.g. ASD, VSD, PDA. This is associated with increased pulmonary plethora.
2. Ventricular enlargement. The shape of heart in ventricular enlargement has already been discussed.
3. Ventricular aneurysm.
4. Pericardial effusion.

### Left to Right Shunt (L → R)

*Radiological Features (Fig. 4.37)*

- Look at the X-ray for cardiomegaly. Confirm cardiomegaly by measurement described above.
- Look at the pulmonary conus, if full and convex, indicates pulmonary hypertension.
- Now look at the shape of the heart. See the apex of the heart which is rounded due to enlargement of right ventricle and is being lifted up clear off the diaphragm. As right atrium also enlarges in left to right shunt, the right border looks also rounded and fuller than normal.
- Determine the position of the heart with reference to position of the vertebrae. In left to right shunt (e.g. ASD, VSD) the heart is sometimes shifted transversely to the left and so the right edge of the vertebral column is revealed.



**Fig. 4.37:** Chest X-ray (PA view) shows features of left to right shunt. The X-ray was taken from a patient with ASD (atrial septal defect). There is mild cardiomegaly with large pulmonary artery and enlarged arteries in the hila with plethora in the lung fields. Aortic knuckle is small. The radiological appearance is suggestive of left to right shunt (ASD)

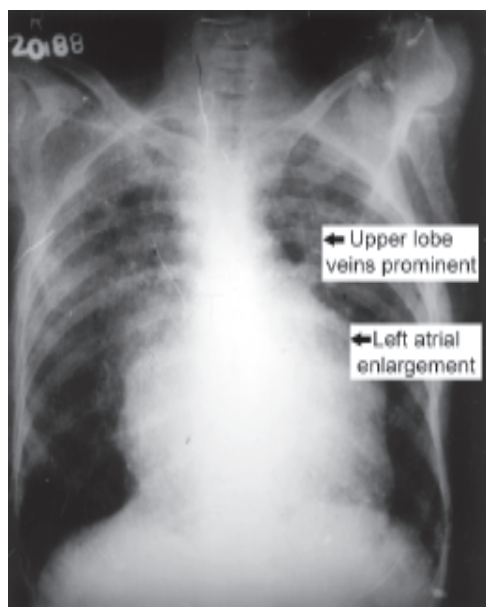
- Pulmonary plethora. In left to right shunt, there is increased blood flow through pulmonary vessels leading to their dilatation called – *pulmonary plethora*. On X-ray, the vessels especially the pulmonary artery and lung vasculature are prominent (i.e. bronchovascular markings are visible up to the periphery) and increased pulsations of these vessels may be seen on fluoroscopy.
- Look at the aortic knuckle and arch of aorta. It is often smaller due to shunting of blood from left side to right side rather than passing through aorta.

### Mitral Valve Disease

Mitral stenosis produces a combination of left atrial and right ventricular enlargement; while mitral regurgitation produces left atrial and left ventricular enlargement; other radiological signs are common to both. The heart in mitral valve disease is called *mitralised heart*.

*Radiological Features (Fig. 4.38)*

- Look at the cardiac shadow which is enlarged in mitral valve disease.
- Look at the left border. Straightening of the left border is due to left atrial enlargement. Sometimes the left atrium enlargement is so great (giant left atrium in



**Fig. 4.38:** Chest X-ray (PA) showing characteristic radiological features of mitral stenosis (mitralised heart). Heart size enlarged with prominent upper lobes veins, left atrial enlargement, double atrial shadow on the right side near the heart border, the apex is dipping into the diaphragm indicate mitralised heart

mitral regurgitation) that this part of the heart bulges outward (*third mogul sign*).

- Now look at the right border of heart. Look carefully for a double atrial shadow which is best seen in well penetrated film and is due to left atrial enlargement (*mitralised heart*). The left atrium also causes the right heart border to shift further over to the right than usual. For left atrial shadow, hold the X-ray in right hand in horizontal or oblique position in front of you in bright light, the double shadow, i.e. double right border will be visible as peripheral less opaque and inner dense opaque area.
- Look at the carina by following the tracheal shadow to its bifurcation into right and left bronchi. The angle between the two bronchi is  $<90^\circ$ . Widening of this angle suggest left atrial enlargement.
- Look at the apex. If it is lifted up clear off the diaphragm, the heart enlargement is right ventricular type. If the heart lies on diaphragm (boot-shaped), then it is left ventricular enlargement.
- Look at the pulmonary area. Prominent pulmonary conus indicates pulmonary hypertension.

- Look at the lung fields and pulmonary vasculature. Prominent upper lobe veins (*inverted mostache sign*), haziness of lung field from hilum towards periphery and the transverse Kerley's B line indicating interstitial oedema indicate pulmonary venous hypertension and acute pulmonary oedema or congestive heart failure.
- Look at the mitral valvular orifice area for flecks of calcification.

### Left Ventricular Aneurysm

A left ventricular aneurysm is a cause of heart enlargement on chest X-ray. It can often cause generalised enlargement of left ventricle and be indistinguishable from left ventricular dilatation.

#### Radiological Features (Fig. 4.39)

- Heart shadow is enlarged
- Look at the left border of heart for a bulge. If a bulge is noticed, follow it to determine whether it imperceptibly merges with the heart border, if yes, then it is suggestive of ventricular aneurysm.
- Now look for calcification in this area. In long – standing aneurysm, a rim of calcification along the heart border may be seen.

### Pericardial Effusion

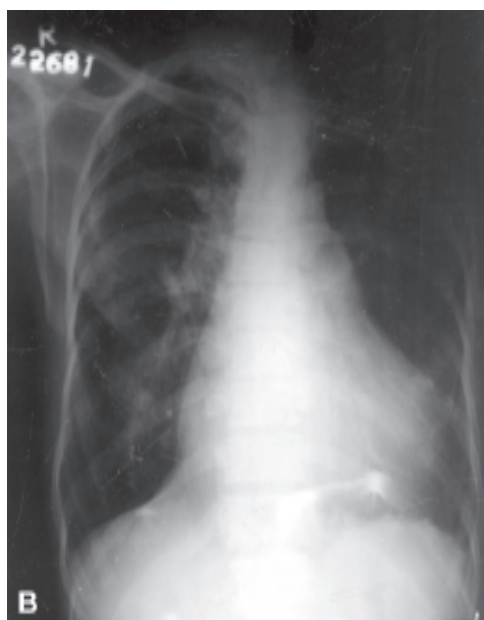
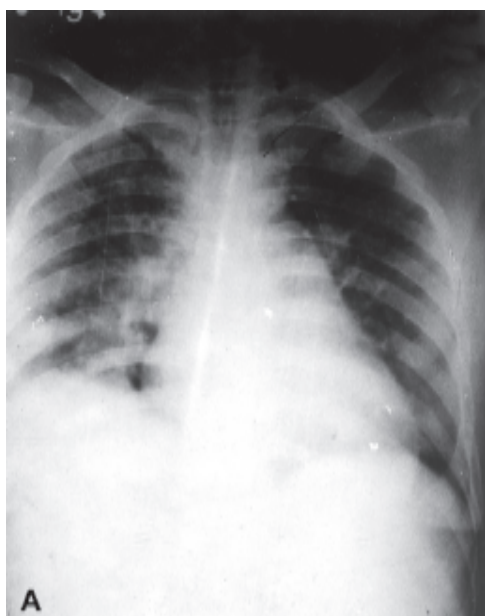
Pericardial effusion means collection of fluid in the pericardial sac leading to enlargement of cardiac shadow on chest X-ray.

#### Causes

They are given in the Table 4.2.

#### Radiological Features (Figs 4.40 and 4.41)

- *Cardiac shadow* is enlarged. Look at the X-ray and confirm the enlargement of cardiac shadow by measurements.
- *Money-bag appearance*. In contrast to chamber enlargement, the heart shadow is globular in shape with straightening of both the borders of the heart. Both the hila are covered by the heart shadow.
- *Lung fields*. In contrast to ventricular enlargement where lung fields are congested and vascular markings

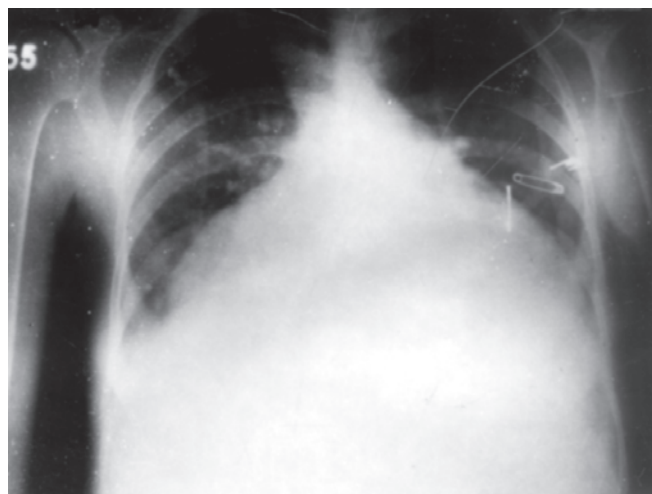


**Figs 4.39A and B:** Chest X-ray (PA view) shows: A. Left ventricular aneurysm. There is enlarged cardiac shadow with a bulge on the lower left border of the heart B. Left ventricular enlargement. The heart is boot-shaped with prominent pulmonary conus (X-ray set for comparison). There is increased bronchovascular marking

prominent near the hilum, the lung vasculature is normal or oligoemic in pericardial effusion.

**Table 4.2:** Causes of pericardial effusion

1. **Transudative**
  - Congestive cardiac failure
2. **Exudative**
  - Infection e.g. viral, bacterial (tuberculosis, pyogenic), amoebic (rupture of amoebic liver abscess into pericardium), fungal (actinomycosis, histoplasmosis)
  - Postmyocardial infarction
  - Neoplastic infiltration
  - Collagen vascular disorders e.g. rheumatoid arthritis, SLE
  - Trauma, postradiation
  - Iatrogenic e.g. postcardiac surgery
  - Metabolic e.g. uraemia
  - Endocrine e.g. myxoedema
3. **Hemopericardium (blood in pericardial cavity)**
  - Trauma
  - Neoplastic infiltration
  - Aortic dissection
  - Bleeding diathesis e.g. leukaemia, anticoagulation



**Fig. 4.40:** Chest X-ray (PA view) showing pericardial effusion. Note the money-bag appearance of the heart with oligoemic lungs

## ABDOMINAL X-RAYS

### How to read an abdominal X-ray?

#### Inspection of X-ray film

Points to be noted are:

- **Technical assessment:** Assessment of date, name, date of birth, age and sex of the patient is essential. Further information gathered is ward No., name of





**Fig. 4.41:** Pleuropericardial effusion. Note the pericardial effusion (heart shadow enlarged with oligemic lungs). In addition, there is peripheral convex opacity rising from the right costophrenic angle, merging with cardiac shadow and emerging above it as convex opacity with concavity towards lung indicating right pleural effusion

the hospital which gives an idea about the problem of the patient being referred i.e. gastrointestinal or genitourinary problem.

- **Projection of the film:** Every abdominal X-ray is an AP film because beam passed from the front to the back with the film behind the patient who is lying down with X-ray machine overhead. On demand, you can have an erect film or even decubitus views. Usually the radiographer will mark the film with a badge or write on it by hand “supine” or “erect” to guide you. Otherwise also, you can guess how a given film was taken from the relative positions of organs, fluid and gas etc.
- **Penetration:** Under-penetration (film is less dark) is not a problem because if you can see the bones in the spine, the most of everything else you need to see will probably be visible as well. However, in any over-exposed film (excessively dark) areas on an X-ray must be inspected with a bright light behind them (there is provision in certain view boxes to see such area(s) or a separate device may be available). However in case of doubt, a good film after full preparation of the patient may be got done again

because certain important information such as air under diaphragm which indicates an potential fatal condition is likely to be missed.

- **Shadows on the X-ray:** It is worth knowing that only five basic densities are visible such as;
  - i. Gas—Black
  - ii. Fat—Dark grey
  - iii. Soft tissue/fluid—Light grey
  - iv. Bone/calcification—White
  - v. Metal—Intense white
- **Visible structures on plain abdominal film**  
On X-rays, the abdominal structures outlined are:
  - i. Solid organs e.g. liver, spleen, kidneys
  - ii. Hollow organs e.g. gastrointestinal tract
  - iii. Bones

These structure can be classified as;

- Visible or not visible and therefore whether present or potentially absent
- Too large or too small
- Distorted or displaced
- Abnormally calcified
- Containing abnormal gas, fluid or discrete calculi

#### *Indications of plain X-ray abdomen*

1. For stone and calcification in the genitourinary area, pancreas, solid organ, haematomas, abnormal mass (lymph nodes), vascular structures etc.
2. Perforation of hollow organ e.g. stomach, colon, appendix etc. Erect film will show air under diaphragm.
3. Duodenal or paralytic ileus/or gallstone ileus. Dilated intestinal loops are seen.
4. Subdiaphragmatic pathology. An amoebic liver abscess may push right dome of the diaphragm and a big spleen will push left dome. In ascites, both domes are raised on supine X-rays.
5. Eventration of diaphragm: The gastric contents are seen in thoracic cavity in eventration of left dome.
6. Certain soft tissue masses e.g. psoas abscess, paravertebral abscess.

#### *Importance of X-ray abdomen*

Look upon X-ray as an extension of physical examination and regard the radiological signs as equivalent to physical signs in clinical medicine.



Remember that the X-ray is only a snapshot of the patient and that serious disease may still be present despite a normal initial X-ray. Follow up films are thus necessary to come at a correct diagnosis as the radiological signs evolve.

Never forget to get the X-ray reported by a radiologist because he/she is trained to see and extract the maximum amount of useful information from every film that can frequently help to optimize the care of your patient.

Always provide the radiologist with clear, full, legible and accurate clinical information. This will enhance the diagnostic value of the films you have requested and, thus, helps to improve the quality of care of your patients.

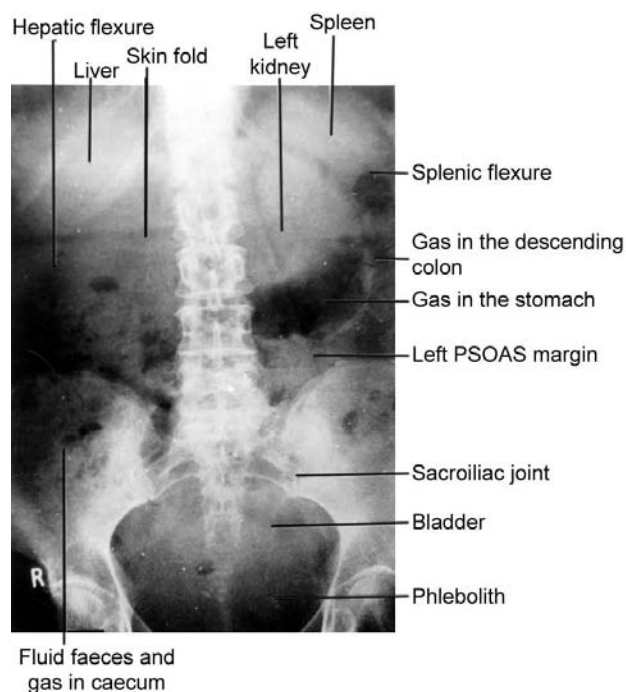
Never try to subject the pregnant female to X-ray examination. If in doubt, either delay the investigation or use ultrasound to investigate the problem.

### Normal adult supine AP X-ray abdomen

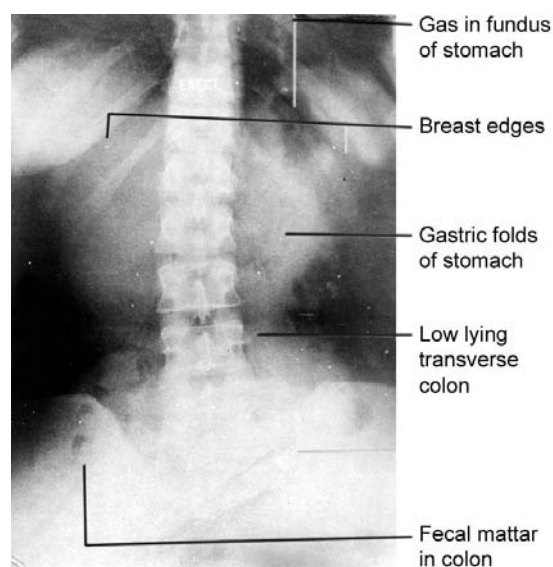
This is the film frequently taken as it shows most of the structures to the best advantage. An X-ray should always be inspected on a view box as irregular illumination and reflection will prevent 10-20 per cent of the useful information on it being visualized.

Look at the film (Fig. 4.42) for;

- Bones e.g. spine, pelvis, lower ribs and the sacroiliac joints.
- The dark margins outlining the liver, spleen, kidneys, bladder and psoas muscles—this line is of an intra-abdominal fat.
- Gas in the body of the stomach and descending colon.
- The wide pelvis indicating the X-ray belong to a female.
- Pelvic phleboliths—a common normal finding.
- Joint spaces of the hip—look for any narrowing or any other abnormality.
- Always look for 'R' mark written anywhere on the film, usually low down on the right side. All references to right or left refers to patient's right and left.
- Lastly check that 'R' marker is compatible with visible anatomy e.g.
  - Liver on the right
  - Left kidney higher than right
  - Stomach bubble on the left

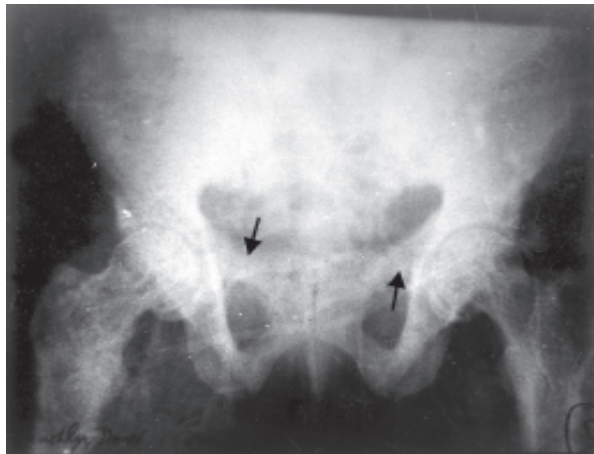


**Fig. 4.42A:** Plain X-ray abdomen of a normal adult (AP supine film) female



**Fig. 4.42B:** Plain normal erect abdominal X-ray in an adult female

**Figs 4.42 A and B:** Adult supine AP radiograph of a middle aged patient



**Fig. 4.43:** Osteomalacia. The X-ray pelvis taken from a patient of chronic renal failure. There is a decrease in bone density and thinning of the cortices. The pseudofractures or looser's zones (radiolucent bands) are indicated by arrows which are perpendicular to the bone

- Spleen on the left
- Heart on the left if visible
- Dark skin fold going across the upper abdomen is normal.

### ABNORMALITIES OF SUPINE X-RAY FILM

#### Vertebral column and pevis

Look at the bones and sacroiliac joint (Fig. 4.43)

Look at the X-ray (Fig. 4.44)

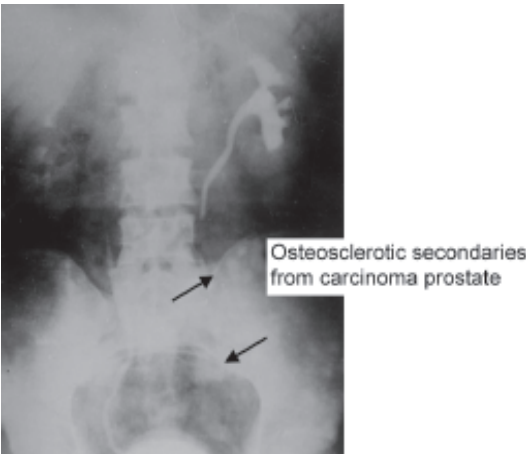
The bones (vertebral and pelvic bones) shows multiple dense foci. These are typical osteosclerotic secondaries (metastases) from carcinoma of prostate. The causes of increase bone density are given in Table 4.3.

**Table 4.3:** Differential diagnosis of increased density of the bones

- Fluorosis—(Fig. 4.47)
- Chronic renal failure
- Paget's disease of the bone
- Osteosclerotic secondaries from prostate (Fig. 4.44)
- Milk-alkali syndrome

Look at the Spine (Figs 4.45 and 4.46)

Figure 4.45 shows biconcave vertebrae (cod-fish deformity). Figure 4.46 shows vertebral column looking



**Fig. 4.44:** Osteosclerotic secondaries from carcinoma prostate. The patient had IVP for hypercalcaemia for renal stones, was found to have multiple dense foci in the pelvis and vertebrae, i.e. secondaries

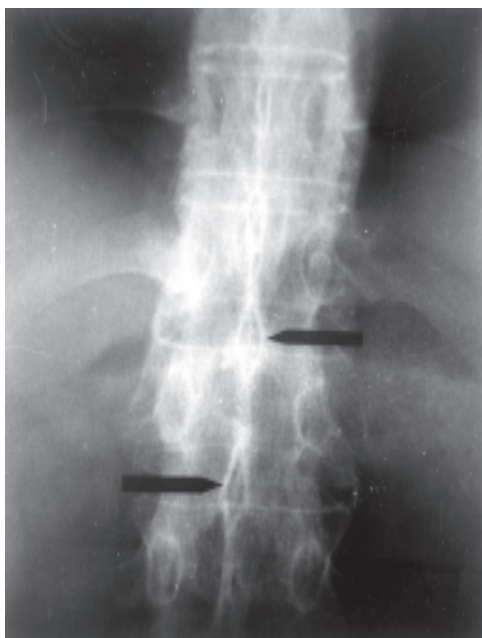
like a bamboo-spine due to calcification of interspinal ligaments.

#### The Kidneys

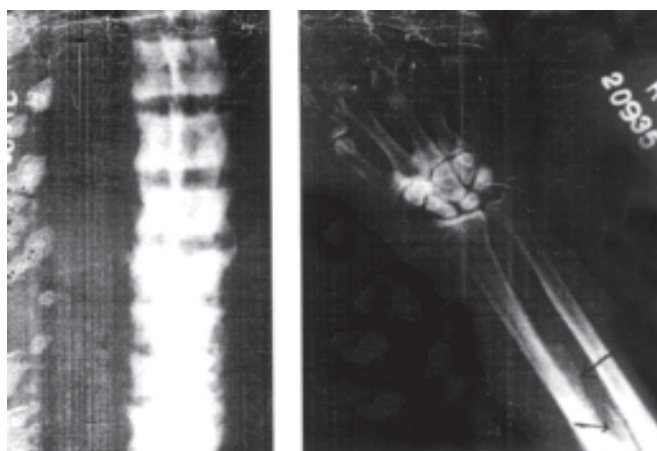
These are usually seen as bean-shaped objects of soft tissue density high in the abdomen. These are smooth in



**Fig. 4.45:** Osteoporosis. There is cod-fish vertebral bodies (e.g. biconcave because of weakening of subchondral plates and expansion of intervertebral discs)



**Fig. 4.46:** Ankylosing spondylitis. Note the calcification of interspinous ligaments producing "Bamboo-spine"



**Fig. 4.47:** Skeletal fluorosis. A. X-ray spine shows increased bone density with calcification of interspinous ligaments. B. X-ray forearm shows calcification of interosseous membrane (→)

outline extending from the upper border of T<sub>12</sub> on the left side to the lower border of L<sub>3</sub> on the right side, with the left kidney lying slightly higher than the right by about 1.5 cm. Both kidneys are inclined medially. Normally, they move down with inspiration and dropping several centimetres in the erect position. Usually, however, only

parts of their outlines are visible and you have to make or deduce its outlines.

#### *Preparation*

For X-ray of urogenital system, the patient is put on low residue diet for 2-3 days. On the night previous to X-ray patient is given a purgative and a deflatulent e.g. methyl polysiloxane or activated charcoal. Patients is kept on overnight fasting.

### **ABNORMALITIES OF KIDNEYS**

#### **A. Big Kidneys (Fig. 4.48)**

- The kidney outlines are enlarged smoothly. The left kidney is slightly larger than the right, although duplex kidney (i.e. one with a double drainage system) may look bigger but histologically it is normal.
- The kidney may be enlarged on one side or on both side (read the causes in Table 4.4).
- The importance of detecting large kidneys is that they may be potential for recovery when this finding is associated with renal failure. Biopsy is required for confirmation of the diagnosis. Ultrasound is done to



**Fig. 4.48:** Plain X-ray abdomen showing large kidneys

exclude renal obstruction and to assess renal parenchyma before biopsy.

- On the other hand, small kidneys (Table 4.5) represent to end-stage renal disease (e.g. irreversible state) making biopsy potentially hazardous, hence, small kidneys constitute contraindication for biopsy.
- Look at the edges of the kidneys whether smooth or lobulated. Irregular kidney outlines indicates scarring of kidneys due to pyelonephritis or glomerulonephritis.

**Table 4.4:** Causes of enlarged kidneys

<i>Bilateral</i>	<i>Unilateral</i>
<ul style="list-style-type: none"> <li>• Acute glomerulonephritis</li> <li>• Diabetic glomerulosclerosis</li> <li>• Adult polycystic disease</li> <li>• ATN</li> <li>• Acute cortical necrosis</li> <li>• Bilateral acute pyelonephritis</li> <li>• Leukaemic infiltration</li> <li>• Lymphomatous infiltration</li> <li>• Amyloid kidneys</li> <li>• Secondary renal disease</li> <li>• Excessive beer drinking</li> </ul>	<ul style="list-style-type: none"> <li>• Acute obstruction</li> <li>• Renal vein thrombosis</li> <li>• Acute pyelonephritis</li> <li>• Radiation nephritis</li> <li>• Duplex system</li> <li>• Compensatory hypertrophy from contralateral nephrectomy or dysfunction</li> <li>• Renal mass</li> </ul>

**Table 4.5:** Causes of small kidneys

<ul style="list-style-type: none"> <li>• Chronic glomerulonephritis</li> <li>• Chronic renal ischaemia (renal artery atherosclerosis)</li> <li>• Chronic pyelonephritis</li> <li>• Reflux nephropathy</li> <li>• Infarctions of kidneys</li> <li>• Senile atrophy</li> <li>• Bilateral congenital hypoplasia</li> </ul>
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### ABNORMALLY PLACED KIDNEY (FIG. 4.49)

Horse-shoe kidney tends to lie lower than the normal. The pathognomonic radiological sign is to see the renal cortices of the lower kidneys on plain X-ray crossing the margins of the psoas muscles medially to connect with the other side with isthmus. The drainage system is malrotated forwards, best seen on the intravenous pyelography (Fig. 4.49).



**Fig. 4.49:** IVP showing horse shoe kidney (Lt)

### The Hollow Organs

#### 1. Stomach (X-ray to be taken in erect position-AP erect)

In the supine position, the gas in the stomach will rise anteriorly and the fluid in the stomach will pool posteriorly creating a circular outline which can be confused with gastric pseudotumour. This mass can be made to disappear by taking X-ray in upright or erect position. In the erect film, the gas bubble will be seen with a fluid level beneath the left dome of diaphragm.

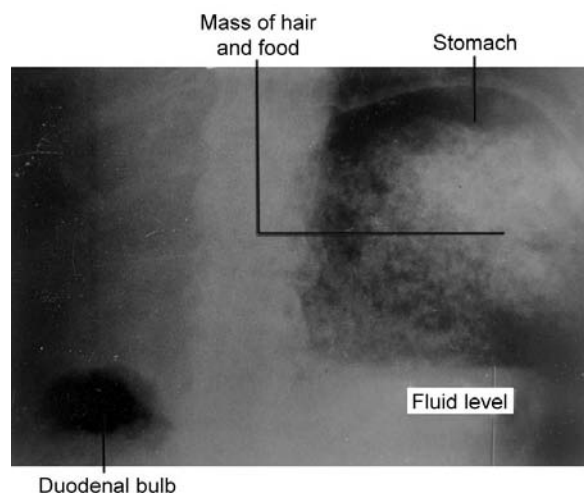
### Abnormalities

#### A gastric outlet obstruction

Look at the X-ray and note

- Abnormal large size of the gastric outline
- Excessive quantities of semidigested food in the stomach
- Small quantity of gas in the small bowel
- Two fluid levels, one on the left under the left dome of diaphragm and other on the right in the right hypochondriac region representing the duodenum. This double-bubble sign indicates high gut obstruction probably in the duodenum.





**Fig. 4.50:** Trichobezoar. There is a mass of hair mixed with food particles retained in the stomach which is dilated due to outflow obstruction (double bubble sign indicates high gut obstruction)

NB: This sign may also be seen in neonates with duodenal atresia.

The semidigested food residue and a fluid confirms obstruction.

NB: A bezoar (Fig. 4.50) looks like semidigested food e.g. phytobezoar-means retained vegetable matter and trichobezoar means hair ball in the stomach.

#### Q. What are causes of gastric outlet obstruction?

- Healed peptic ulcer
- Antral gastric carcinoma
- Lymphoma
- Gastritis
- Tuberculosis (lymph nodes producing obstruction from outside)
- Impacted foreign body
- Bezoar (hair ball, vegetable matter)
- Metastases producing compression from outside

#### Q. What are the clinical signs of pyloric obstruction?

The signs are;

- Increased peristalsis from left to right
- Abdominal distension
- Vomiting
- Succussion splash

#### Small Intestinal Obstruction/Paralytic Ileus

Small bowel pathology usually manifests itself on plain X-ray by abnormal accumulation of gas and fluid due to either functional (i.e. adynamic ileus) or truly mechanical (dynamic) obstruction. The differentiation between small bowel from large bowel obstruction is difficult on plain X-ray but following points help:

1. The large bowel obstruction is peripheral and contains faeces and gas; while small bowel obstruction is central and contains fluid and gas.
2. The more distal the obstruction (large bowel obstruction), the more distended loops will be seen.

Note:

- i. Small fluid levels can be seen normally. Large fluid levels >3 indicate gut obstruction
- ii. The longer the duration of the obstruction, the bigger the fluid levels.
- iii. It is not necessary for obstruction to have fluid levels.

Caution: For fluid levels, always take either an erect or decubitus film

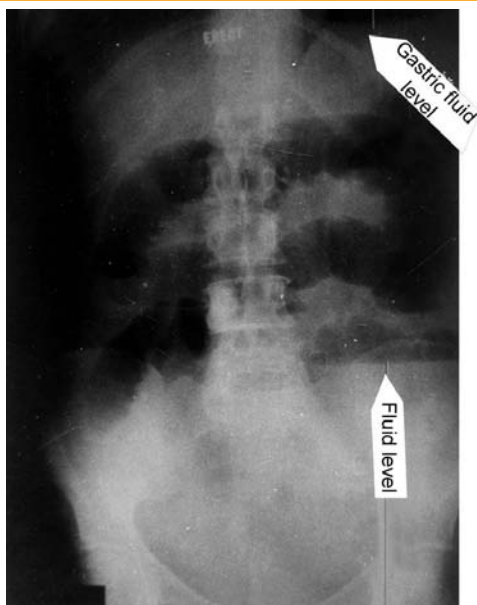
#### Plain X-ray (Fig. 4.51) shows;

- Multiple centrally placed loops of intestine distended with gas and have fluid levels, indicate small gut obstruction.
- Dilated loops of gut in peripheral parts of the abdomen without any fluid level indicate large gut obstruction (Fig. 4.52).

NB: Although obstruction and perforation usually present separately and clinically differently, but it is hard to differentiate between the two on radiological grounds. The clinical context is essential to differentiate between them. However, remember;

- i. Paralytic ileus produces air and fluid levels at one level (i.e. same level); while in the intestinal obstruction, air and fluid level follow a step-ladder pattern or there are rising fluid levels
- ii. Combined small and large bowel dilatation form the classical radiological signs of paralytic ileus while a gas under diaphragm indicates perforation.





**Fig. 4.51:** Small intestinal obstruction. Plain X-ray abdomen (AP-erect film) shows multiple centrally placed loops of distended gut with gas. There are multiple fluid levels

**Q. What are the causes of small intestinal obstruction?**

The causes in different age groups are;

*Adults*

- Post operative adhesions
- Bowel strangulation (band, internal hernia)
- Hernia
- Tumour-lymphoma
- Crohn's disease
- Gallstone ileus

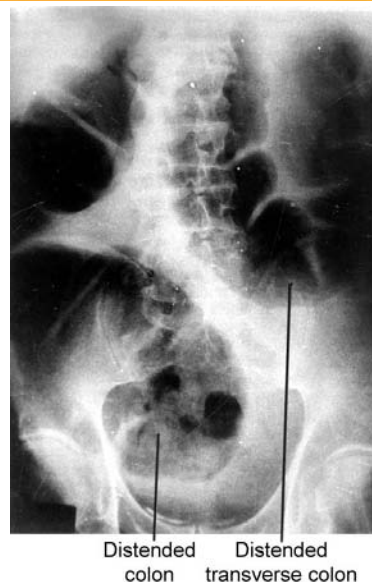
*Children*

- Hypertrophic pyloric stenosis
- Intussusception
- Duodenal atresia
- Meconium ileus

**Q. What are the causes of paralytic ileus?**

The causes are;

- Postoperative e.g. following excessive handling of the gut
- Hypokalaemia
- Drugs e.g. L-dopa
- Peritonitis
- Infarction of the gut
- Trauma
- Reflex ileus from acute abdomen (renal colic, leaking aorta)



**Fig. 4.52:** Plain X-ray abdomen showing large gut obstruction. There is severe abdominal distension with out any fluid levels

**Q. What are the causes large gut (colonic) obstruction?**

The causes are;

- Colon carcinoma
- Diverticulosis
- Volvulus
- Inflammatory bowel disease
- Appendicular abscess
- Metastases
- Lymphoma
- Pelvic masses

**Q. What are the causes of pseudointestinal obstruction?**

The causes are;

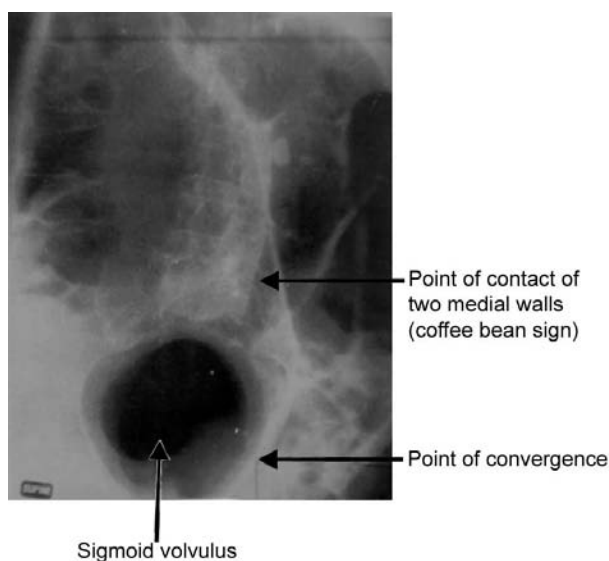
- MI with pulmonary oedema
- Pneumonia
- Myxoedema

**SIGMOID VOLVULUS**

Sigmoid volvulus is grossly dilated sigmoid colon, occurs in elderly patients who have redundant loops of sigmoid colon and a history of constipation. Acute volvulus presents with severe pain, constipation and on PR examination the rectum is empty.

Look at the plain X-ray abdomen (Fig. 4.53 supine AP view): The radiological signs are;

- A grossly dilated loop of sigmoid colon filling the whole abdomen extending from the pelvis to



**Fig. 4.53:** Sigmoid volvulus. Plain X-ray abdomen (AP supine film) shows a grossly distended loop of sigmoid colon extending from pelvis to diaphragm. Coffee bean sign and point of convergence support the diagnosis which is confirmed by retrograde contrast study (barium enema) which will show a “twisted beak-like” or “bird of prey” sign at the point of convergence

diaphragm is seen. Compression together of two medial walls is producing “coffee bean sign”

- There is lack of haustra due to enormous distension
- The following signs help to the diagnosis and indicate severity of distension.
- a. The apex of distension of colon lies above the 10th thoracic vertebra
  - b. Convergence of lower margins of the distended loops on the left
  - c. Liver overlap sign indicates presence of distended colon above the liver on the right
  - d. Left flank overlap sign indicates distended loop in the left flank

NB: Absence of free air under diaphragm rules out perforation

### Calcification in Abdomen

The calcification on abdominal X-ray is seen because of;

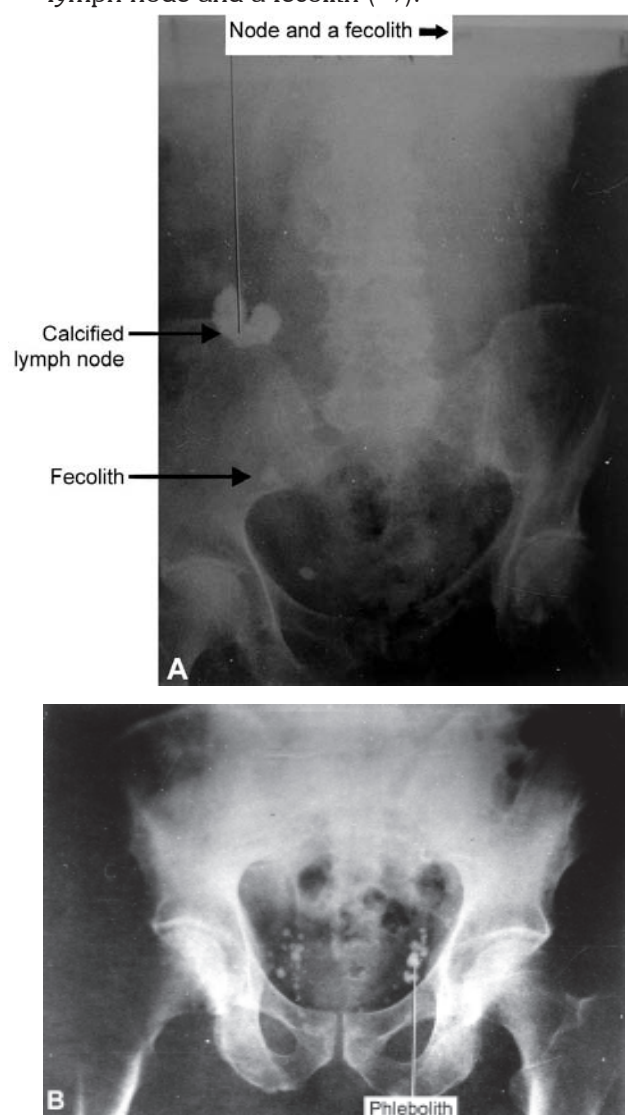
- Fecoliths
- Phleboliths
- Calculi e.g. renal, biliary, pancreatic

- Calcification seen in liver, e.g. amoebic liver abscess, tuberculosis, rim of calcification outlining the hydatid cyst, histoplasmosis
- Calcified lymph nodes
- Calcification of abdominal wall, cysticercosis

### Calcified Faecoliths

Look at X-ray (Fig. 4.54B)

- A cluster of faecoliths or phleboliths are present which are calcified. These are not lymphnodes. These are in the region of colon. Figure 4.54A shows a calcified lymph node and a fecolith (→).



**Figs 4.54A and B:** A. Calcified lymph nodes. Note a calcified shadow in right iliac region due to calcified lymph node. There is a faecolith (→), B. Phleboliths in the region of colon and rectum

### Calcification of Aorta (Aortic Aneurysm)

Calcification of aorta/aortic aneurysm is common in old, in patients with diabetes and chronic renal failure.

**NB:** Always look for abdominal aorta when you are looking at plain X-ray of abdomen because calcification of aorta/aortic aneurysm may be an incidental finding. Secondly it is important from therapeutic point of view as this condition is potentially and eminently treatable by surgery or stenting.

Look at the Figure 4.55: The plain X-ray abdomen shows;

- Typical thin rim of calcification in the wall of the aorta. Most aneurysms bulge to the left (commonly) or to the right (occasionally) or lie in the midline over the spine (uncommonly)

*Clinical tip:* A normally calcified aorta (due to atherosclerosis) over the spine with parallel or converging walls excludes an aortic aneurysm (e.g. aortic aneurysmal calcificational means loss of parallelism in its walls). Therefore, always look at the walls of aorta for parallelism.

### Q. What are causes of aneurysm of aorta and other vessels?

The causes are;

- Atherosclerosis

- Hypertension
- Infection (mycotic)
- Traumatic
- Congenital
- Fibromuscular dysplasia
- Polyarteritis nodosa

### Caution

The absence of a visible aneurysm on the plain film does not mean the patient has not got one. Always try other sophisticated investigations to confirm its presence or absence.

### Calcified lymph nodes

#### A. Mesenteric lymph nodes

Look at the Fig. 4.56. The plain X-ray abdomen shows;

- There are many granular opacities in the flanks
- There is a cluster of opacities over the L3/4/5 lumbar spine levels
- There are some further opacities in the epigastrium.

*Conclusion:* These are calcified lymph nodes because;

- These are numerous



**Fig. 4.55:** Calcification of abdominal aortic aneurysm. Plain X-ray abdomen showing a large calcified mass bulging to the left



**Fig. 4.56:** Calcified mesenteric lymph nodes. There is cluster of opacities over mid-lumbar region (L3/4/5 spine) one both sides of spine

- They lie in line with mesentery
- They tend to be quite mobile and show dramatic change in position from film to film

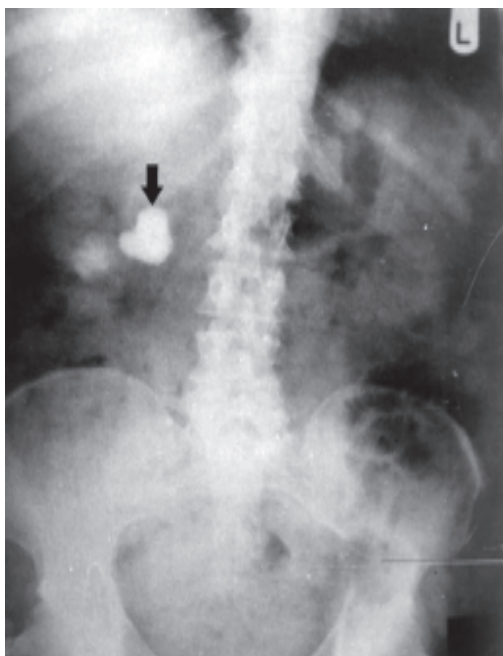
#### Differential Diagnosis

The calcified lymph nodes in mesentery have to be differentiated from calculi and calcification in the underlying organs (kidney, spleen, aorta) right along the side of the spine or iliac vessels. They have to be differentiated from faecoliths/phleboliths.

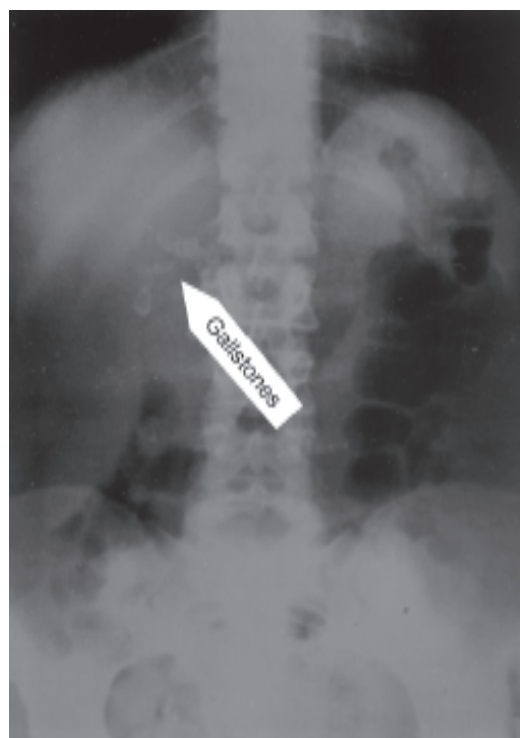
*Para-aortic lymph nodes:* These are seen as spotty calcification along the paravertebral gutter in the upper part of abdomen. In lateral view, these calcified retro-peritoneal lymph nodes, may overlie the spine, require to be differentiated from calculi or renal calcification.

#### Renal stones/calculi

The majority of stones (90% approx) that form in kidneys are radiopaque (Fig. 4.57) owing to their calcium content. They are seen on plain X-ray as radiopaque opacity/opacities ranging from tiny (nephrocalcinosis) to one big calculus blocking the collecting system (stag-horn).



**Fig. 4.57:** Renal stone. Plain X-ray abdomen shows radiopaque calculus at the right pelvic ureteric junction (↓)



**Fig. 4.58:** Plain X-ray abdomen showing radiopaque gallstones (uncommon). They are usually diagnosed on USG

Note: A renal stone maintains the constant position in relation to kidney when erect or oblique films or control tomography films are taken. The renal stone has to be differentiated from calcified costal cartilage or a gallstone (Fig. 4.58) both of which are anteriorly placed structures. Always remember that gallstones are anterior to the spine while the shadow of renal stone is superimposed on vertebral column in lateral film.

#### Q. What are the causes of renal calculi?

The causes are;

- Hyperparathyroidism
- Infection
- Urinary tract obstruction
- Dehydration
- Hypervitaminosis D
- Medullary sponge kidney
- Uric acid stones
- Renal tubular acidosis
- Milk-alkali syndrome
- Renal tuberculosis





**Fig. 4.59:** Calcification of the pancreas on plain X-ray abdomen in chronic pancreatitis

### Pancreatic Calcification

Pancreatic calcification occurs in chronic pancreatitis, cystic fibrosis and occasionally in pancreatic tumours.

Plain X-ray abdomen (Fig. 4.59) shows fine punctate foci of calcification lying from the right of the upper lumbar spines passing upwards and obliquely to the left to the region of the splenic hilum. This is pancreatic calcification.

### BARIUM STUDY

Barium contrast study is useful to delineate the interior of gastrointestinal tract when it is filled with radiopaque substance e.g. barium (Fig. 4.60).

Barium meal is done by asking the patient to swallow a suspension of barium. The radiologist observes the movements of the barium on the fluorescent screen or on the TV monitor of an image intensifier. Films are taken at different intervals depending on the site of pathology detected or suspected. These films provide a permanent record of any abnormality.

A plain X-ray of the abdomen should always be taken before barium study in patients with suspected perforation/obstruction.

Normal barium meal study will reveal normal plica semilunaris (Fig. 4.60).

- Barium swallow is done for any pathology in the oesophagus i.e. varices (Fig. 4.61), stricture, cardia



**Fig. 4.60:** Normal barium meal study

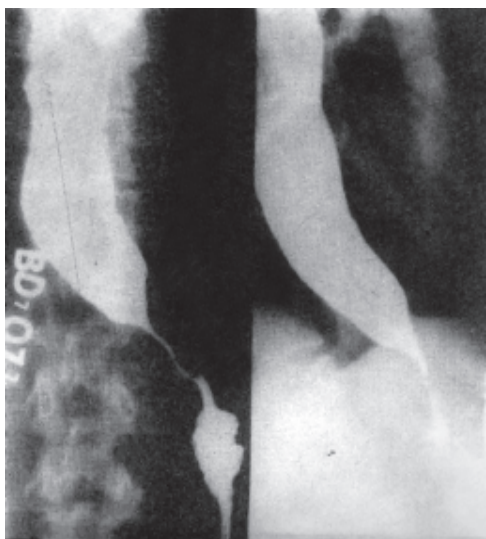


**Fig. 4.61:** Barium swallow showing oesophageal varices (→)

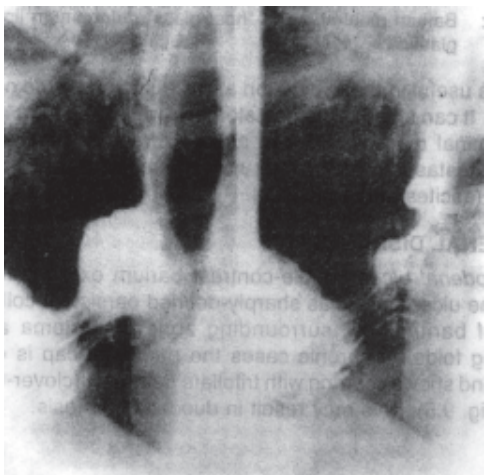
achalasia, (Fig. 4.62) hiatus hernia (Fig. 4.63) and malignancy.

- The barium study is done for certain gastric disorders by taking films of the abdomen at intervals after a barium meal. Abnormalities in the transit time to the colon and in small bowel pattern e.g. dilatation, narrowing, flocculation of barium are seen in





**Fig. 4.62:** Barium swallow showing “parrot-beak” appearance of distal oesophagus with proximal dilatation suggestive of cardia achalasia



**Fig. 4.63:** Barium swallow showing sliding hiatus hernia

malabsorption. Areas of narrowing with proximal dilatation, fistulae and mucosal abnormalities are seen in Crohn's disease. Small bowel diverticula or neoplasm may also be seen. Narrowing of ileocaecal junction with caecum being pulled up indicates ileocaecal tuberculosis (Fig. 4.64).

### Barium Enema

For this study, barium suspension is introduced via a tube into the rectum as an enema and manipulated around



**Fig. 4.64:** Ileocaecal tuberculosis. There is narrowing of ileocaecal junction and caecum is pulled up

the rest of the colon to fill it. The radiologist screens the barium filled colon and films are taken for permanent record. The barium is then evacuated and further films are taken.

By this study, obstruction, polyps (Fig. 4.65), pseudopolypoidosis (Fig. 4.66) of the colon, tumours, diverticular disease (Fig. 4.67), fistulae and other abnormalities of rectum (Fig. 4.68) can be recognised.

Following evacuation, air is introduced into the colon. This facilitates visualisation of the mucosa by distending the colon, hence, is specially useful for detecting small lesions e.g. polyps and small tumours, which may be missed on barium study. This type of study in which barium and air are used for contrast is called “double contrast study”.

### INTRAVENOUS PYELOGRAPHY

It is excretion urography in which a radio-opaque iodine compound is injected intravenously and its excretion through the kidney is followed at certain intervals. It is important investigation for assessing renal functions in renal failure and for structural abnormalities such as



**Fig. 4.65:** Barium enema showing numerous rounded filling defects suggestive of polyps



**Fig. 4.67:** Barium enema showing diverticulosis



**Fig. 4.66:** Barium enema showing diffuse pseudopolyps in a patient with chronic ulcerative colitis



**Fig. 4.68:** Barium enema showing “apple-core” deformity in carcinoma rectum

calculi or obstruction. When renal function is poor, the kidneys are more easily seen if tomographs and large dose of the contrast are used.

This technique provides excellent delineation of the collecting system and ureters and is superior to ultrasound for examining renal papillae, stones and urothelial malignancy.

### Precautions

- Before injecting the dye, iodine sensitivity should be tested
- Resuscitative equipment (drugs, O<sub>2</sub>) should be made available on the side table
- The patient should not take water after the previous night. However, patients with diabetes, myeloma, old age, compromised renal function should be well hydrated to avoid nephrotoxicity due to the contrast medium.
- If patient is taking diuretics, they should be omitted for 3 days prior to the procedure.

### Procedure

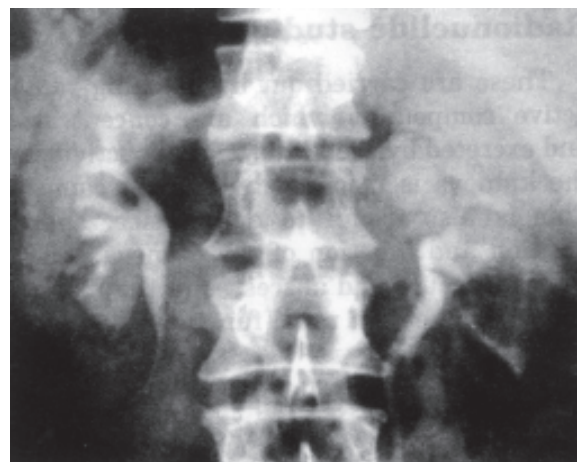
Abdominal binder is applied tightly enough to compress the ureters. Twenty to 40 ml of contrast medium along with an antihistamine is injected slowly I.V. Abdominal radiographs are taken at 1,3,5,10,15 and 30 minutes intervals, the binder is then released and at 45 minutes 'prone' and 'standing' films are taken. Bladder is visualised in the film taken when the patient gets a sensation of fullness and desires to empty it.

A radiogram (micturating cystogram) is taken during and immediately after evacuation of the bladder.

### Results and interpretation

Normal IVP visualises both the kidneys and ureters very well (Fig. 4.69):

1. *Nephrogram*: It means appearance of the contrast in the kidneys. Normally, a good nephrogram should be seen in one minute film. Nephrogram is delayed and contrast is poor if renal function is impaired.
  - In renal artery stenosis, late appearance of the nephrogram and hyperconcentration of the contrast is seen
  - Nephrogram will appear late, persists for longer period and will progressively show hyperconcentration of contrast in acute unilateral urinary tract obstruction
2. *Visualisation of kidneys*: The kidneys are visualised as bean-shaped organs situated each on either side in paravertebral region between L<sub>1</sub> to L<sub>4</sub>. The abnormalities seen are;
  - i. Pitted scars or small contracted kidney in pyelonephritis
  - ii. Polycystic kidneys give bumpy outline with stretched pelvicalceal system giving spidery leg appearance
  - ii. Cysts would cast a negative shadow
3. *Visualisation of pelvicalceal system*: The normal calyces are cup-shaped structures. The abnormalities seen are;
  - i. Clubbed calyceal system indicate hydronephrosis [unilateral (Fig. 4.70) or bilateral]. There may be a non-functioning kidney (Fig. 4.71).

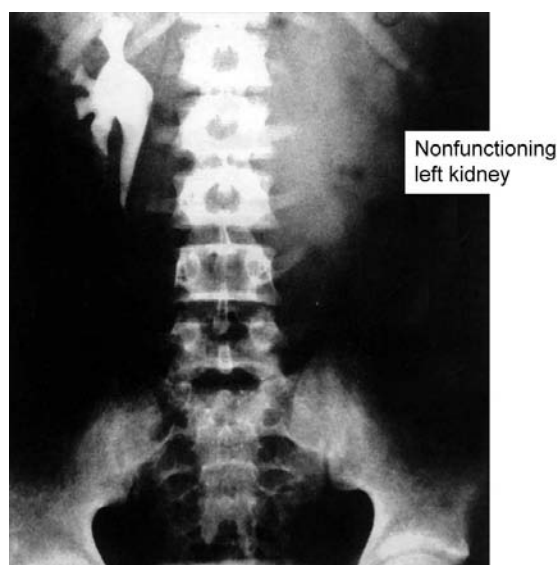


**Fig. 4.69:** Normal intravenous pyelogram: Both kidneys and upper part of both ureters are well outlined by contrast



**Fig. 4.70:** Hydronephrosis of left kidney due to obstruction at pelviureteric junction





**Fig. 4.71:** Intravenous pyelography: The left kidney is not visualized by contrast (non-functioning left kidney). The right kidney shows normal pelvicalyceal system

- ii. In acute papillary necrosis, sloughed off papillae may cause ring shadows on IVP. Acute papillary necrosis is seen in analgesic nephropathy, sickle cell nephropathy, chronic interstitial nephritis and diabetes.
4. *Visualisation of ureters:* The ureters are outlined when the contrast is excreted through the ureters to the bladder. The ureters are thin tubes arising from the pelvis of the kidneys and ending into the urinary bladder. The abnormalities are;
  - Ureter(s) may be dilated proximal to the urinary tract obstruction due to stone, tumour, retroperitoneal growth or pelvic masses, ureteric stricture etc. They may also look dilated with the use of antispasmodic, oral contraceptives and pregnancy.
  - They are narrowed in infection. Retroperitoneal fibrosis pulls one or both of them towards mid-line and produces its narrowing with proximal dilatation as described above.
  - The beaded appearance of the ureters is seen in renal tuberculosis.
5. *Visualisation of bladder:* The bladder is visualized as a globular structure filled with opaque material in the



**Fig. 4.72:** Vesico-ureteric reflux on micturating cystogram. The bladder has been filled by contrast medium through a urinary catheter (not visible). Even before start of micturition, there was gross vesico-ureteric reflux into widely distended ureters and pelvicalyceal system

suprapubic region, gives an accurate definition of its shape, size and condition of the opening of the ureter and any growth or stone. The abnormalities are;

- A small contracted thumble bladder is seen in tubercular cystitis
- A large bladder indicates neurogenic bladder
- The bladder neck is elevated and there may be convex indentation due to prostate enlargement
- Trabeculations and diverticula are seen in bladder neck obstruction and spastic bladder. Diverticula may also be congenital sometime.

Micturating cystogram is done by introducing a catheter into the bladder and injection of radio-opaque contrast through it. The bladder will be visualised and vesico-ureteric reflux (Fig. 4.72) can be demonstrated in which radio-opaque contrast appears into the ureter(s) during act of micturition or even before micturition. Vesico-ureteric reflux indicates chronic pyelonephritis which has certain additional findings on IVP;

- The kidneys are small, and show pitted scars
- There is clubbing of the calyces adjacent to the contraction of the renal substance.

# 5

# Electrocardiography

## INTRODUCTION

### Definition

Electrocardiography is a graphic recording of the electrical potentials generated and propagated in the heart on a paper by surface electrodes. The electrical events are recorded as waveforms.

### Uses

- Chamber hypertrophy (atrial or ventricular or both)
- Myocardial ischaemia/infarction
- It is a gold standard for diagnosis of arrhythmias
- Conduction defects at various levels, e.g. SA blocks, AV blocks, bundle branch blocks, fascicular blocks
- Myocardial and pericardial diseases
- To study the effects of drugs, electrolytes and poison on the heart
- Evaluation of efficacy of various intervention procedures, e.g. angioplasty, bypass surgery
- Holter's monitoring (dynamic/ambulatory ECG) is used to relate symptoms with ECG while stress (exercise) ECG is used to diagnose asymptomatic coronary artery disease.

The ECG paper is designed with small and large squares such that in one minute 300 large squares or 1500 small squares are covered. One small square is equal to 0.04 sec in duration and 1 mm in height and width. One large square is equal to 5 small squares and is  $5 \times 0.04 = 0.2$  sec in duration. These dimensions help to calculate the heart rate in regular sinus rhythm and in an arrhythmia. The voltage of one small square is 0.1 mV.

### The PQRST and U Complex

An ECG complex depending on the waveform is called *PQRST-U complex*.

The *P wave* signifies atrial depolarisation and repolarisation. It precedes QRS complex.

The *QRS complex* consists of a small negative q wave which, sometimes, may be absent, a large positive R wave and a second small negative S wave. It signifies ventricular depolarisation.

The *T wave* is positive wave which follows QRS after a small interval (ST segment) and signifies ventricular repolarisation.

The *U wave* is the second repolarisation wave, indicates delayed repolarisation, occurs as a small positive deflection after the T wave.

### The ECG Intervals

1. **PR interval** is the time taken by the impulse to travel from SA node to the ventricles.
2. **QT interval** is the time taken by the ventricular events – depolarisation cum repolarisation.

### Junctions and Segments

1. **J point** is the junctional point at which QRS ends with S wave returning to the baseline. This point is an important landmark for evaluation of ST segment deviation (elevation/depression).
2. **The ST segment.** It is the distance between the end of S wave (J point) to the beginning of T wave.

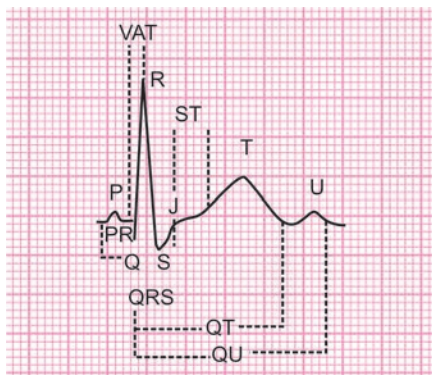
### The 12 Leads of Surface ECG

- Limb leads (bipolar) I, II and III



**Box 5.1:** Points to be noted in ECG

- Standardisation (full, normal or half)
- Voltage
- Rate
- Rhythm
- Axis
- Position
- The P wave
- The PR interval
- The QRS complex
- QRS duration
- ST segment
- T wave
- QT interval
- The U wave



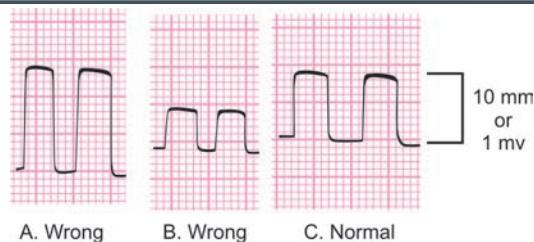
**Fig. 5.1:** A normal ECG complex showing its various components

- Unipolar leads (augmented leads) aVR, aVL and aVF
- The precordial or chest leads: V<sub>1</sub> to V<sub>6</sub>

**INTERPRETATION OF ECG**

The ECG is interpreted with reference to certain points given in the Box 5.1 and Figure 5.1.

1. **Standardisation:** In the beginning of ECG, there is mark of standardisation. Normal standardisation means inscription of a rectangle of 10 mm or 1 mV. Half and double standardisation is to be done in case voltage is high or low respectively. The Figure 5.2 shows the right and wrong standardisation.
2. **Voltage:** There is no clear cut criteria for normal voltage. It is measured from the top to bottom of the complex, i.e. top of R wave to bottom of S wave (Fig. 5.3).
3. **Rate:** The heart rates varies from 60-100/min.
4. **Rhythm:** Normal rhythm on ECG is sinus, i.e. PP and RR intervals are constant and regular. The disturbance in rhythm is called *dysarrhythmia* or *arrhythmia* (these have been discussed further in this section).



**Fig. 5.2:** Standardisation wrong (A & B). Normal (C)

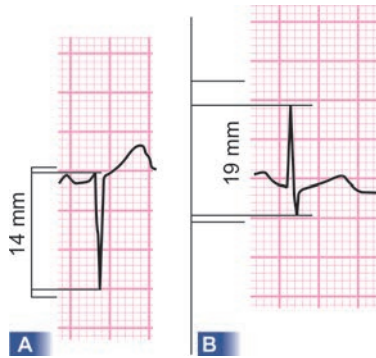
5. **Axis:** The mean frontal plane QRS axis is between 0° to + 90°.
6. **Position:** The heart position is intermediate, i.e. there is R wave in both aVL and aVF.
7. **Rotation:** Normally there is no rotation of the heart. The transition zone (equiphase R and S complex) lies in V<sub>3</sub> or V<sub>4</sub>.
8. **P wave:** The normal P wave is upright, less than 2.5 mm in height and width except in aVR.
9. **PR interval** varies from 0.12 to 0.2 second.
10. **QRS complex:** In standard limb leads (I, II, III) there is dominant R wave. In V<sub>1</sub>, there is smaller r wave with large S wave. There is good progression of R wave height from V<sub>1</sub> to V<sub>6</sub> i.e. R waves goes on increasing and S wave goes on decreasing as one proceeds from V<sub>1</sub> towards V<sub>6</sub>.
11. **QRS duration** is 0.04 to 0.1 sec.
12. **ST segment** normally is isoelectric.
13. **T wave** is upright normally in those leads where QRS complex is upright, i.e. in all leads except aVR and V<sub>1</sub>.
14. **QT interval:** It is measured from the beginning of q wave or R wave (if q wave is absent) to the end of T wave (T wave is included). It varies from 0.35 to 0.44 sec. and depends on the heart rate. The corrected QT (QTc) is calculated by the Bazette formula as follows:

$$QTc = \frac{QT \text{ interval in sec}}{\sqrt{R - R \text{ interval in sec}}}$$

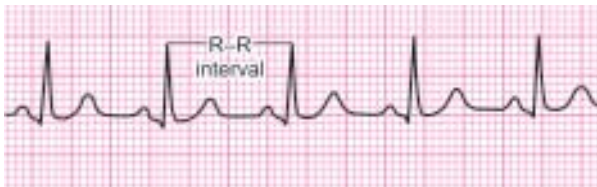
- **U wave.** Normally U wave is not recorded but sometimes may be recorded as a small upright wave after T wave in leads V<sub>2</sub>-V<sub>4</sub> only.

**ABNORMALITIES OF VOLTAGE**

- **The high voltage of QRS** complexes signifies the ventricular hypertrophy (read ventricular hypertrophy).



**Fig. 5.3:** Measurement of voltage:  
A. An RS complex, B. An QRS complex



**Fig. 5.4:** Calculation of heart rate by 1500 method.  
HR is  $1500 \div 16 = 93/\text{min}$  approx

- **Low-voltage graph** means the QRS complex is  $<5$  mm in standard leads (I, II, III, aVR, aVL and aVF). The causes include pericardial effusion, myxoedema, emphysema (COPD), obesity (thick-chested persons), CHF, oedema of the chest wall.

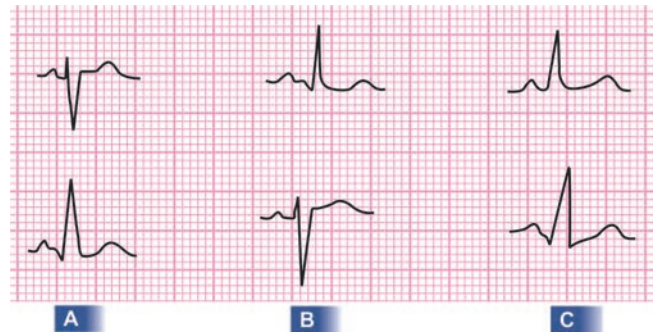
### CALCULATION OF HEART RATE (HR)

It is calculated as follows:

1. **1500 method (Fig. 5.4):** If the rhythm is regular (sinus), then it is calculated by counting the R-R interval in mm (small squares) and dividing the 1500 by the R-R interval (number of small squares). Suppose R-R interval is 20 mm (20 small squares) then heart rate is  $1500 \div 20 = 75$  bpm.
2. **Ten seconds method:** If heart rate is irregular, then count the QRS complexes in a fixed interval, i.e. in 10 seconds and then the number of QRS obtained are multiplied by 6 to get the approximate heart rate per minute.

### ABNORMALITIES OF CARDIAC AXIS

Roughly the cardiac axis is calculated by putting the complex in lead III below lead I and observe the direction of QRS complexes.



**Figs 5.5A to C:** Axis deviation: A. Right axis,  
B. Left axis, C. No axis deviation

### Left Axis Deviation

(axis lies between  $-0^\circ$  and  $-90^\circ$ )

If the complexes are leaving apart, i.e. moving away from each other, then it is left axis deviation (Fig. 5.5B). The causes are:

- Left ventricular hypertrophy
- Left anterior fascicular block
- Inferior wall infarction
- Ventricular pacing
- Ventricular tachycardia
- WPW syndrome
- Endocardial cushion defect
- Cardiomyopathies.

### Right Axis Deviation

(axis lies between  $+90^\circ$  and  $+180^\circ$ )

In this axis deviation, the QRS complexes face each other (right opposite to each other (Fig. 5.5A).

The causes of right axis deviation include:

- Right ventricular hypertrophy
- Acute pulmonary embolism
- Right bundle branch block
- Left posterior fascicular block
- Dextrocardia
- Cor pulmonale (acute or chronic)
- Normal variation, infancy.

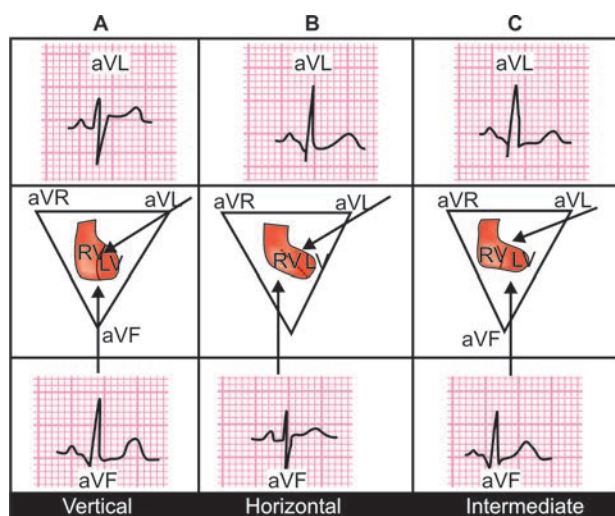
### No Axis Deviation

(axis lies between  $0^\circ$  and  $+90^\circ$ )

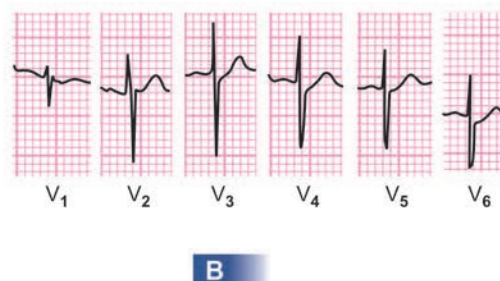
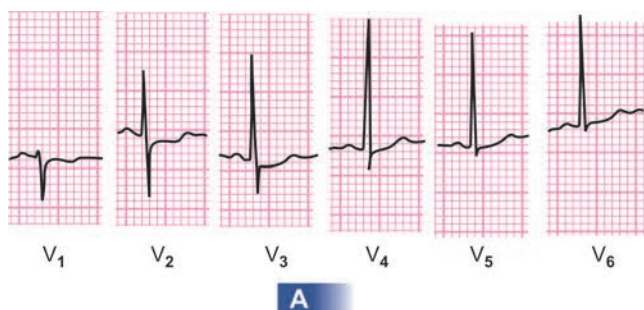
The complexes neither drift away nor face each other but lie in the same upward direction (Fig. 5.5C).

## POSITIONS OF THE HEART

- A. **Vertical position:** It is said to be present if aVF shows major upward deflection and aVL shows major downward deflection (Fig. 5.6). This position is associated with clockwise rotation of the heart and right axis deviation, hence, the conditions causing right axis deviation will lead to it.
- B. **Horizontal heart position** (QRS deflection is upwards in aVL and downward in aVF) (Fig. 5.6). This position is associated with left axis deviation and counterclockwise rotation, hence, conditions causing left axis deviation are associated with it.
- C. **Intermediate heart position** (normal heart position). In this position, both the leads aVL and aVF show major upward deflection (Fig. 5.6).



**Fig. 5.6:** Various positions of the heart: A. Vertical, B. Horizontal, C. Intermediate



**Fig. 5.7:** Rotation of the heart: A. Counterclockwise, B. Clockwise

## ELECTRICAL ROTATION OF THE HEART

The heart rotates on horizontal axis either clockwise or counterclockwise and decides its position. Vertical heart corresponds to the clockwise rotation; and horizontal heart position to counterclockwise rotation. The rotation is decided by shifting of the transition zone. The transition zone is constituted by that precordial lead which exhibits an equiphasic RS complex ( $R = S$  wave). Normal transition zone lies in mid-precordial leads e.g.  $V_3$ - $V_4$  (Fig. 5.7).

- A. **Clockwise rotation:** The transition zone shifts towards  $V_5$ - $V_6$  which means the lead  $V_5$  or  $V_6$  or both exhibit RS complexes.
- B. **Counterclockwise:** The transition zone shifts towards  $V_1$ - $V_2$ , i.e. the leads  $V_1$  or  $V_2$  shows the equiphasic RS complex.

## THE ABNORMALITIES OF PQRS COMPLEX

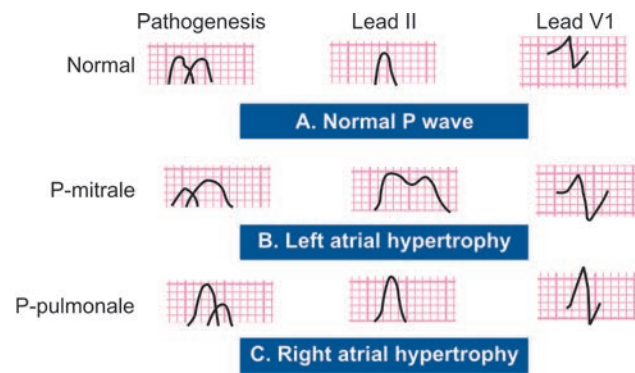
### Abnormalities of P wave

#### (Atrial hypertrophy/enlargement)

The P wave represents atrial depolarisation and repolarisation, hence, reflects atrial hypertrophy and enlargement (Fig. 5.8). The various abnormalities of P wave are:

1. **The P mitrale:** (Wide, bifid P wave  $>2.5$  mm). It is seen in left atrial enlargement. The leads reflecting this abnormality are II, III and aVF and  $V_1$ .
2. **The P pulmonale:** (Tall peaked P wave  $>2.5$  mm in height). It indicates right atrial hypertrophy. It is seen in leads II, III, aVF and lead  $V_1$ .
3. **Absent P waves:** It occurs in atrial fibrillation.
4. **Inverted P wave:** P wave is inverted in leads II, III and aVF in retrograde conduction (e.g. AV nodal arrhythmias) and in lead I in dextrocardia.





**Fig. 5.8:** Normal vs abnormal P waves: A. Normal, B. Left atrial hypertrophy (P-mitrale), C. Right atrial hypertrophy (P-pulmonale)



**Fig. 5.9:** Left ventricular hypertrophy



**Fig. 5.10:** ECG showing right atrial and ventricular hypertrophy

**Table 5.1:** Causes of ventricular hypertrophy

Condition/Cause	LVH	RVH
Congenital heart disease	VSD, PDA, Coarctation of aorta	Pulmonary stenosis, tetralogy of Fallot, Eisenmenger's syndrome
Valvular heart disease	Mitral regurgitation, MVPS, AS and AR	Mitral stenosis, Tricuspid regurgitation
Outflow obstruction	Left ventricular outflow, e.g. aortic stenosis, coarctation of aorta	Right ventricular outflow, e.g. pulmonary stenosis
Hypertension	Systemic hypertension	Pulmonary hypertension, Cor pulmonale (acute or chronic)
Myocardial disease	Cardiomyopathies	Right ventricular dysplasia, right sided cardiomyopathy
Hyperkinetic circulation	Beri-beri, and other high output states	Nil

### Causes of Atrial Enlargement

Atrial enlargement is usually secondary to its corresponding ventricular enlargement, hence, left atrial hypertrophy occurs in those conditions where there is LVH and right atrial hypertrophy in those conditions, where there is RVH (Read causes of ventricular enlargement). In mitral stenosis there is left atrial hypertrophy with right ventricular hypertrophy.

## THE QRS COMPLEX ABNORMALITIES

### Ventricular Hypertrophies (lengthening of QRS complex)

In ventricular hypertrophy, there is increase in height of the R wave in leads representing the hypertrophied ventricle and a corresponding deep S wave in leads representing the nonhypertrophied ventricle. In addition there are associated ST-T wave changes. These changes are due to increase in thickness of free walls of the ventricles with delay in conduction of electrical forces. The causes of ventricular hypertrophy are tabulated (Table 5.1).

The leads to be seen in ventricular hypertrophy are:

$V_1$  = represents the right ventricular forces

$V_5$  = represents the left ventricular forces

### Left Ventricular Hypertrophy (LVH)

The ECG changes are as follows (Fig. 5.9):

1. Increased amplitude of QRS (Voltage Criteria for LVH). As the lead  $V_5$  represents the left ventricle,

hence, the increased voltage  $>27$  mm is seen in this lead in LVH; corresponding to this, a deep S wave will be recorded in lead  $V_1$  representing the non-hypertrophied left ventricle, hence, criteria for LVH are:

$R$  in  $V_5 > 27$  mm

$RV_5 + SV_1 > 35$  mm

This criteria is valid in persons above the age of 35 years

2. There is increase in ventricular activation time interval between beginning of the Q wave to top of the R wave (normal being 0.03 to 0.05 sec) and duration of QRS (0.06 to 0.09 sec) is increased.
3. There is ST segment depression and T wave inversion in leads representing hypertrophied left ventricle ( $V_5$ ,  $V_6$ ).
4. There is left axis deviation.
5. Counterclockwise rotation.

The **Romhilt** and **Estes** point scoring system for LVH (Box 5.2).

#### Box 5.2: Scoring system for LVH (Romhilt and Estes criteria)

• Increased voltage	3 points
• ST-T changes	3 points
• P wave indicative of left atrial enlargement (wide P wave, i.e. P mitrale)	3 points
• Left axis deviation (LAD)	2 points
• Increased VAT	1 point
• Widened QRS	1 point

Note: At least 5 points are required to establish the diagnosis of LVH



**Right Ventricular Hypertrophy (RVH—Fig. 5.10)**

- i. The R wave is more than S wave in  $V_1$ , i.e.  $R > S$  or  $R : S > 1$ .
- ii. There is persistence of deep S wave in  $V_5$  and  $V_6$ , i.e. there is RS pattern in  $V_5$ - $V_6$ .
- iii. There is ST segment depression and T wave inversion in leads  $V_1$ - $V_2$ .
- iv. There is right axis deviation, vertical heart position and clockwise rotation.

**Biventricular Hypertrophy (Fig. 5.11)**

The ECG criteria are:

- LVH ( $R > 27$  mm in  $V_5$  or  $RV_5 + SV_1 > 35$  mm) plus right axis deviation and clockwise rotation.

**OR**

LVH in  $V_5$  and  $V_6$  ( $R > 27$  mm) plus RVH in lead  $V_1$  ( $R = S$  wave) plus a *Katz-Wachtel phenomenon* (large RS complexes) in  $V_3$ - $V_4$ .

**OR**

RVH plus left axis deviation provided other causes of left axis deviation have been excluded.

- An rSR' pattern (abnormal QRS) whose duration is  $> 0.12$  sec in lead  $V_1$  and or  $V_2$  (Fig. 5.12).
- There is corresponding deep S wave in  $V_5$ - $V_6$ .
- VAT in leads  $V_1$ - $V_2$  is prolonged.
- There is associated ST segment depression and T wave inversion in leads  $V_1$ - $V_2$ .
- There is right axis deviation.

Tip: A wide ( $> 0.12$  sec) rSR' pattern in  $V_1$ - $V_2$  is sufficient to make the diagnosis of RBBB.

**Causes**

1. *Congenital*, e.g. common in children
2. *Acquired*
  - Coronary artery disease
  - Cardiomyopathies
  - Hypertensive heart disease
  - Congenital heart disease (ASD, VSD)
  - Acute cor pulmonale
  - Myocarditis
  - Idiopathic.

**Left Bundle Branch Block (LBBB)**

The ECG characteristics are (Fig. 5.13):

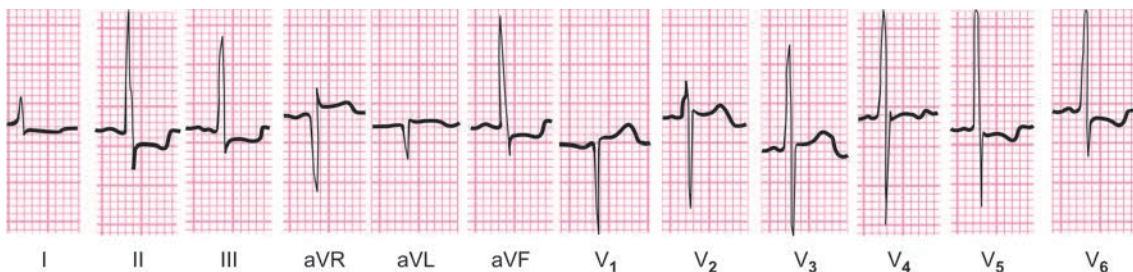
- i. Q wave is absent in normal Q-wave containing leads (e.g. I, aVL,  $V_5$ - $V_6$ ).
- ii. The QRS in leads  $V_5$ - $V_6$  is either slurred (R, RR' or notched R) or RSR' pattern. There is QS pattern in  $V_1$ .
- iii. QRS duration is  $> 0.12$  sec in leads  $V_5$ - $V_6$ .
- iv. VAT is increased in the same leads  $V_5$ - $V_6$ .
- v. There is associated ST segment depression and T wave inversion in leads  $V_5$ - $V_6$ .

**BUNDLE BRANCH BLOCK (BBB)**

Bundle branch block is defined as delay or block in conduction through a bundle branch (right or left) of bundle of His. It is characterised by wide QRS complex  $> 0.12$  sec in duration. The upper limit of normal QRS is 0.10 sec.

**Right Bundle Branch Block (RBBB)**

It is characterised by;



**Fig. 5.11:** Biventricular hypertrophy. There is right axis deviation  $+75^\circ$ . The R and S waves are of equal amplitude but larger than normal in lead  $V_3$  and  $V_4$  with voltage criteria of LVH ( $RV_5 + SV_1 > 35$  mm). The good R wave in  $V_2$  indicates RVH. All these criteria suggest biventricular hypertrophy



**Fig. 5.12:** Right bundle branch block (RBBB). The ECG shows right axis deviation and vertical heart position. There is wide ( $> 0.12$  sec) QRS (rsR') pattern in lead  $V_1$  which is diagnostic of bundle branch block. There is persistence of wide slurred S wave in  $V_5$ - $V_6$



**Fig 5.13:** Left bundle branch block. The ECG shows a wide slurred R wave in leads I, aVL,  $V_5$  and  $V_6$ . There is associated ST depression in these leads. There is left axis deviation and horizontal heart position

The leads to be seen in BBB and the differentiation between RBBB and LBBB are given in Table 5.2.

**Causes of LBBB**

- Coronary artery disease
- Cardiomyopathy and myocarditis
- Hypertensive heart disease
- Aortic valve disease
- Drugs, e.g. quinidine.

**FASCICULAR BLOCKS**

The heart has three fascicles. LBB consists of two fascicles, (i) *left anterior* and (ii) *left posterior*. The RBB itself acts as a single fascicle. The combination of RBBB with block in one of the fascicles of LBB is called

**Table 5.2:** Differentiating pattern of QRS in BBB

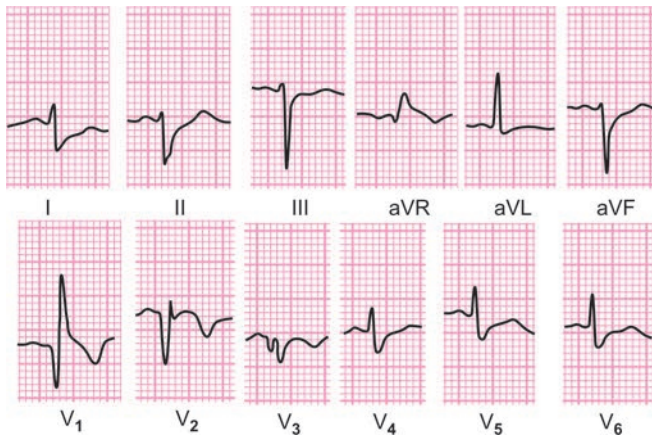
Leads to be seen	RBBB	LBBB
$V_1$	rSR'	QS
$V_5$	qRS	Slurred R or RR' or RSR'

*bifascicular block*. Conduction delay through one of the fascicle is called *fascicular block*.

The fascicular blocks are characterised by respective axis deviations. The duration of QRS in these blocks is either normal or gets slightly prolonged but does not exceed 0.11 sec in any case.

**Left Anterior Fascicular Block**

It is characterised on ECG by left axis deviation  $> -30^\circ$  resulting in rS pattern in leads II, III and aVF. The



**Fig. 5.14:** Bifascicular block. There is RBBB with left axis deviation  $> -30^\circ$

combination of left anterior fascicular block with RBBB is called *bifascicular block* (Fig. 5.14).

### Left Posterior Fascicular Block

It is characterised on ECG by abnormal right axis deviation  $> +110^\circ$  resulting in qR pattern in leads II, III and aVF and rS pattern in lead I.

### ABNORMALITIES OF T AND U WAVE

The T wave is dome-shaped wave with two limbs and asymmetric peak, follows the QRS in each lead after ST segment. It is normally upright in all leads except leads III and aVR,  $V_1$  and  $V_2$ .

### Abnormalities of the T Wave

- *Inverted in myocardial ischaemia.* There is symmetrical inversion of T wave in subendocardial infarction or non-Q wave MI. Asymmetric T wave inversion occurs in ventricular hypertrophy with strain, bundle branch blocks, electrolyte disturbance, myocarditis, cardiomyopathies, CVA, digitalis toxicity and pulmonary embolism.
- *Tall and peaked T waves* occur in hyperkalaemia and true posterior wall myocardial infarction.
- *Flat or low voltage T waves* occur in thick chest-walled persons, emphysema, pericardial effusion, myxoedema, myocarditis, myocardial ischaemia, hypokalaemia, hypocalcaemia, hypoventilation, etc.

### Abnormalities of U Wave

It is transiently inverted in:

- Angina (inversion of U wave on stress test indicates ischaemia)
- Acute pulmonary embolism
- Left ventricular overload
- Digitalis effect.

### ABNORMALITIES OF INTERVALS

#### The P-R Interval

P-R interval is measured from the beginning of the P wave to the beginning of QRS complex (if q wave is absent then R wave of QRS).

Normal P-R interval is 0.12 to 0.20 sec.

#### Abnormalities

The P-R interval is;

- *Short:* Short P-R interval indicates accelerated conduction, is seen in nodal ectopics, nodal rhythm, WPW syndrome and LJT syndrome.
- *Variable:* Varying P-R intervals are seen in wandering atrial pacemaker.
- *Prolonged:* Prolonged P-R interval indicates first degree heart block (Read heart blocks).

#### The P-P and R-R Intervals

The P-P and P-R intervals are regular in normal sinus rhythm. The P-P interval is used to calculate the atrial rate and R-R interval is used to calculate the ventricular rate. In 1:1 AV conduction, the atrial and ventricular rates are equal and regular. In heart blocks, some of the P waves are conducted while others are blocked, hence, the P-P interval becomes different than R-R interval.

#### Abnormalities

1. P-P interval is not equal to R-R interval in second degree AV block. P-P interval is halved than R-R interval in 2:1 AV block.
2. No relation of P-P to R-R interval in complete heart block.
3. The P-P interval varies in multifocal atrial tachycardia and wandering atrial pacemaker.



### The QTc Interval

It is measured from the beginning of QRS complex to the end of T wave.

Normal interval is 0.39 to 0.44 sec.

It is corrected for heart rate, called QTc. The normal QTc is <0.40 sec in males and less than 0.45 sec in females.

The causes of long and short QTc are given in Table 5.3.

**Table 5.3:** Causes of long and short QT (QTc)

#### Long QTc

- A. *Physiological*-during sleep
- B. *Congenital* prolonged QT syndromes, e.g.
  - The Jervell-Lange-Nielsen syndrome
  - Romano-Ward syndrome
- C. *Acquired*
  - Hypocalcaemia
  - Myocarditis
  - Acute MI
  - Drugs, e.g. quinine, quinidine, procainamide
  - Antidepressants
  - Head injury with intracranial bleed
  - Hypothermia
  - Hypertrophic cardiomyopathy
  - Advanced or complete AV block
  - Ventricular tachycardia-torsade de pointes

#### Short QTc

- Digitalis effect
- Hyperthermia
- Hypercalcaemia
- Vagal stimulation

### The ST Segment

The ST segment is measured from the J point (the point at which S wave becomes isoelectric) to the beginning of T wave. The deviation of ST segment (elevation/depression) is decided with reference to a TP line – a straight line joining the termination of T wave and the beginning of the P wave.

Normal ST segment is either:

- Isoelectric OR
- Depressed by 0.5 mm in precordial leads OR
- Elevated upto 2 mm in precordial leads in Negroes

### Abnormalities

1. The horizontal ST segment depression > 80 m sec on stress testing indicates positive test for provokable ischaemia.
2. Sagging ST segment or ST segment depression with downward-sloping indicates coronary artery disease.
3. Mirror image of correction mark type of ST segment is seen in digitalis effect and its toxicity.
4. Raised ST segment with convexity upwards indicates myocardial injury e.g. myocardial infarction.
5. Raised ST segment with concavity upwards is seen in myopericardial disease, e.g. myocarditis, pericarditis.

### Causes of ST Segment Elevation and Depression

Table 5.4 enlists the causes of ST segment elevation and depression.

### MYOCARDIAL INFARCTION (ST ELEVATION MI-STEMI)

The myocardial infarction consists of three zones (Fig. 5.15), i.e. **ischaemia – injury – necrosis** sequence which on ECG is characterised:

- i. **ST segment elevation** (represents the central zone of injury Fig. 5.15)

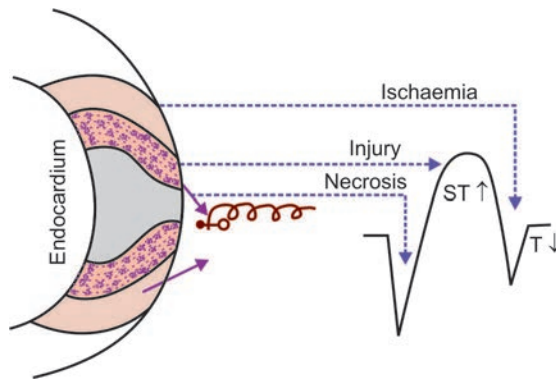
**Table 5.4:** Causes of deviation of ST segment

#### 1. ST segment elevation

- Acute myocardial infarction
- Prinzmetal's angina
- Ventricular aneurysm
- Pericarditis
- Early repolarisation syndrome
- Hyperkalaemia
- Cardiac tumour

#### 2. ST segment depression

- Acute subendocardial infarction
- Unstable angina (non ST-elevation MI)
- Myocarditis or cardiomyopathies
- Digitalis effect and toxicity
- Left ventricular hypertrophy and strain
- Bundle branch block
- Electrolyte disturbance
- CVA
- Pulmonary embolism



**Fig. 5.15:** Necrosis—injury—ischæmia sequence of acute myocardial infarction: ST ↑ = ST elevation; T ↓ = T wave inversion

- ii. **Pathological Q waves** (represents central area of necrosis Fig. 5.15)
- iii. **The asymmetric T wave inversion** represents outmost zone of ischaemia.

The myocardial infarction is diagnosed on ECG by ST elevation, Q waves and T wave inversion, in more than two consecutive leads (Figs 5.16A to D).

The infarction pattern (q wave, ST elevation and T wave inversion) seen in different leads determines its site, i.e. anterior, inferior, posterior or lateral wall (Table 5.5).

## MYOCARDIAL ISCHAEMIA

The deep symmetrical/asymmetrical inversion of T wave during an episode of pain indicates myocardial ischaemia (Figs 5.17 and 5.18). Angina means pain during exertion relieved by rest; is an example of myocardial ischaemia, may or may not be associated with T wave inversion. Normal ECG with symptoms of angina warrants stress

testing. Positive stress test means horizontal ST segment depression  $\geq 1$  mm staying for  $> 80$  msec in more than 2 leads (Fig. 5.19).

## RHYTHM DISTURBANCES

### Sinus Rhythm and its Abnormalities

The SA node maintains a normal regular rhythm of the heart called *sinus rhythm*. The SA node is under the influence of autonomic system, can accelerate and decelerate its heart rate.

### Sinus Bradycardia (Fig. 5.20)

Box 5.3 depicts the causes of bradycardia.

### Sinus Tachycardia (Fig. 5.21)

*Tachycardia* ( $HR > 100/\text{min}$ )

The tachycardia may be sinus (normal acceleration of heart rate) or may be due to an arrhythmia (disturbance of cardiac rhythm – Read cardiac arrhythmias). The tachycardia may also be supraventricular or ventricular tachycardia. The causes of sinus tachycardia are:

- Anxiety states, excessive use of tea or coffee, smoking
- Hyperthyroidism
- Acute pulmonary embolism
- Circulatory failure
- Congenital heart disease
- Drug induced (adrenaline, thyroid hormone therapy, nicotine, alcohol), atropine, nifedipine, ACE inhibitors)
- Congestive cardiac failure
- Physiological in neonates and during REM sleep.

### Sinus Arrhythmia (Fig. 5.22)

It refers to alternate periods of slow and rapid heart rates. If heart rate becomes faster during inspiration and slower during expiration, then it is called *sinus respiratory arrhythmia*.

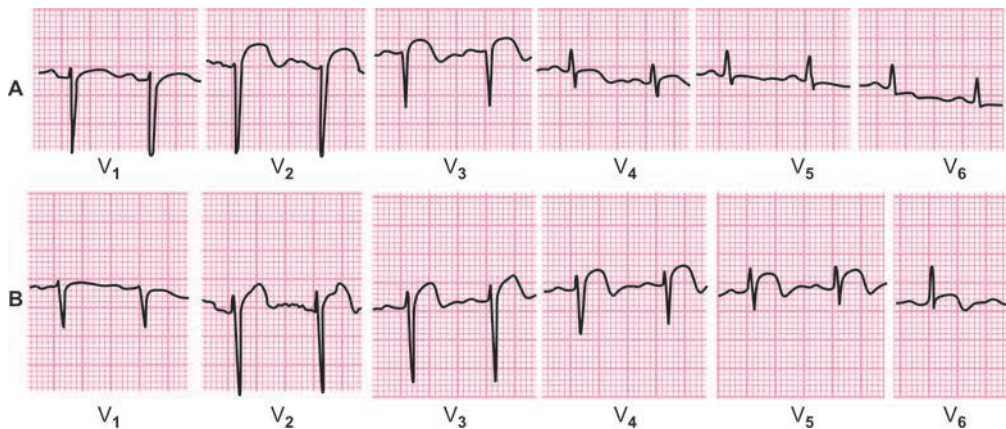
### Supraventricular Arrhythmias

Conveniently, a tachyarrhythmia can be classified into two main categories depending on the site of origin, i.e.

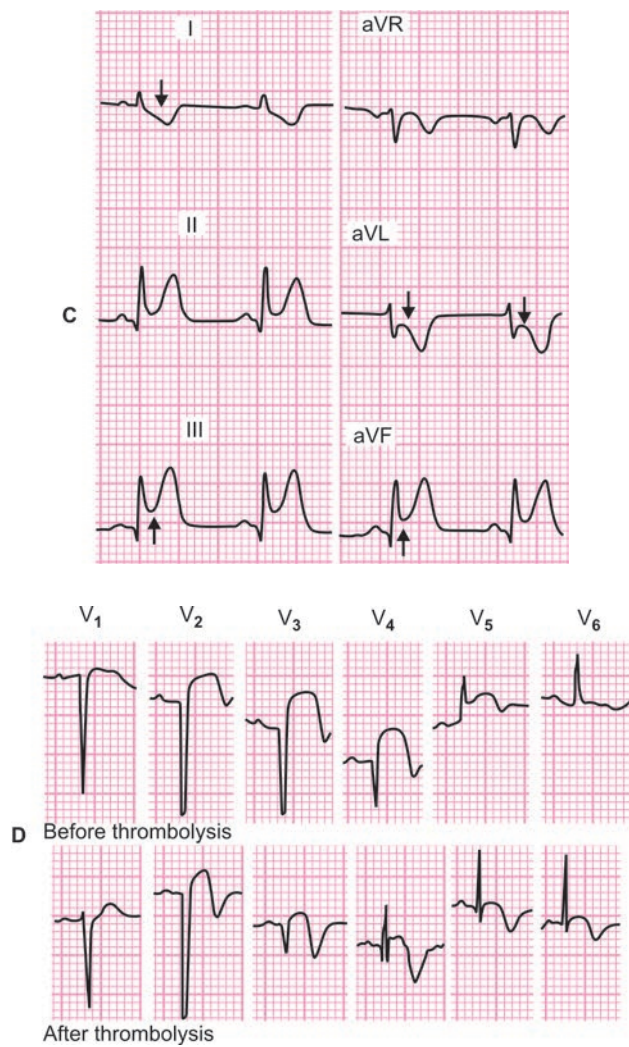
**Table 5.5:** Various sites of infarction and leads involved

Site of infarction	Infarction pattern (Q wave, ST elevation and T wave inversion) on leads involved
Anteroseptal	V <sub>1</sub> -V <sub>4</sub>
Extensive anterior	I, aVL, V <sub>1</sub> -V <sub>6</sub>
Inferior	II, III, aVF
Lateral	I, aVL, V <sub>5</sub> -V <sub>6</sub>
Posterior	Note: Instead of infarction pattern / reciprocal changes of infarction are seen

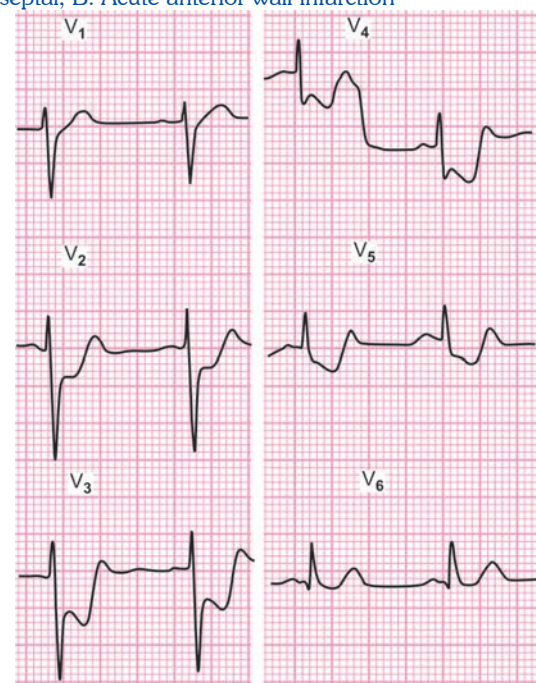




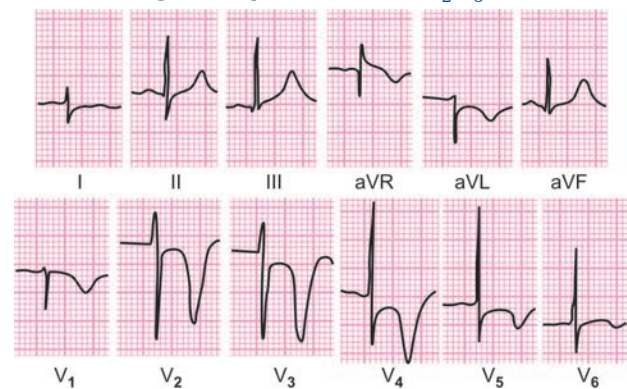
**Figs 5.16A and B:** Myocardial infarction: A. Anteroseptal, B. Acute anterior wall infarction



**Figs 5.16C and D:** Myocardial infarction: C. Inferior wall infarction, D. Acute MI before and after thrombolysis. There is resolution of ST segment by 75%

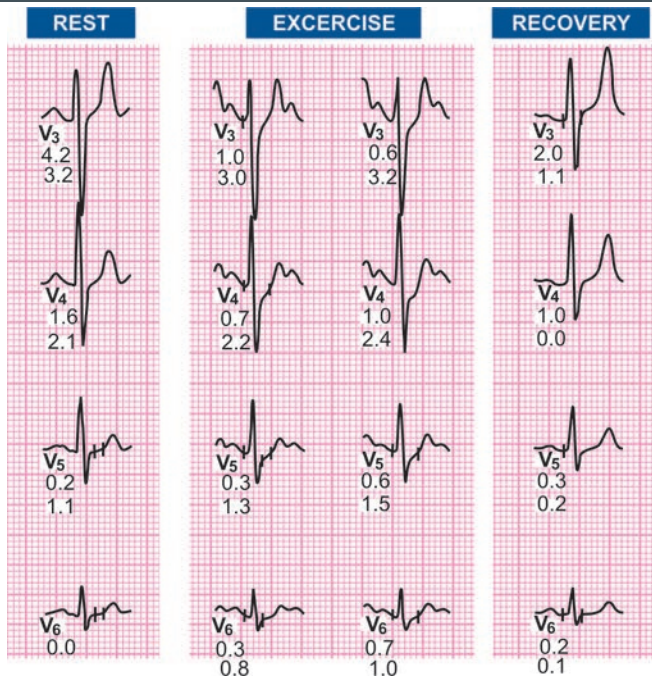


**Fig. 5.17:** Acute anterior myocardial ischaemia. There is ST segment depression in leads V<sub>2</sub>-V<sub>5</sub>



**Fig. 5.18:** Acute subendocardial ischaemia/infarction. Note symmetric T wave inversion in leads V<sub>1</sub>-V<sub>5</sub>

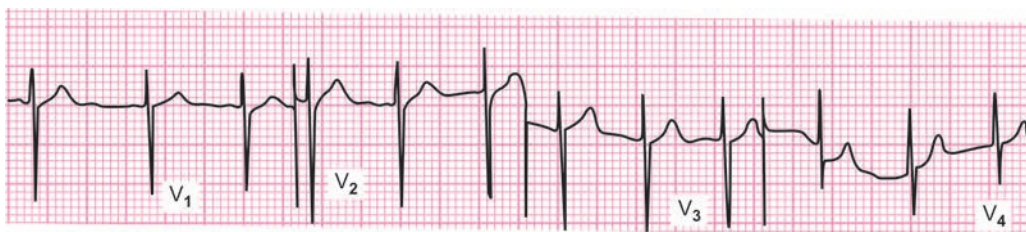




**Fig. 5.19:** Positive stress test. Note the ST segment depression  $> 1$  mm staying for  $> 80$  msec during peak exercise and during recovery in leads  $V_3$ - $V_6$



**Figs 5.20A and B:** Sinus bradycardia: A. Resting heart rate is 38/min (approx) regular indicating sinus bradycardia, B. After atropine challenge, heart rate is doubled (75/min regular) indicating vagotonia as the cause of bradycardia



**Fig. 5.22:** Sinus arrhythmia. There is marked change in R-R interval ( $> 0.08$  sec) in the same lead. This is due to respiratory effort, hence, called respiratory sinus arrhythmia—a normal phenomenon

### Box 5.3: Causes of bradycardia

Bradycardia (HR  $< 60$ /min/min). It is seen in following conditions:

1. Physiological (athlete, vagotonic person)
2. Hypothyroidism
3. Obstructive jaundice
4. Hypothermia
5. Sick sinus syndrome
6. Electrolyte disturbance, e.g. hyperkalaemia
7. Inferior wall infarction
8. Drugs (digoxin, betablockers, calcium channel blockers)
9. Heart blocks
10. Raised intracranial pressure
11. Uraemia
12. Poisoning (OP compounds, ALP poisoning, scorpion bite, etc)
13. Hyperactive carotid sinus



**Fig. 5.21:** Sinus tachycardia. Heart rate is  $(1500/12) = 125$ /min regular

- I. Supraventricular (originating from a focus situated above the ventricle, may be in the atria or AV node)
- II. Ventricular (focus of excitation lies in the ventricle)

**Supraventricular arrhythmias** include:

- *Supraventricular ectopics* (atrial or nodal)
- *Paroxysmal supraventricular tachycardia*. It includes sinus, atrial or AV nodal re-entrant tachycardia and automatic atrial tachycardia.
- *Atrial flutter and atrial fibrillation*.

## Supraventricular Ectopics

### Causes

- Sometimes occasional ectopic is a normal finding
- Anxiety state; excessive use of tea, coffee, alcohol
- Heart disease, e.g. heart failure, coronary artery disease, valvular heart disease, and hypertensive heart disease
- Thyrotoxicosis
- COPD and chronic cor pulmonale
- Systemic infections
- Drugs, e.g. digitalis, amphetamine, adrenaline, thyroxine replacement therapy.
- Electrolyte imbalance, e.g. hypokalaemia

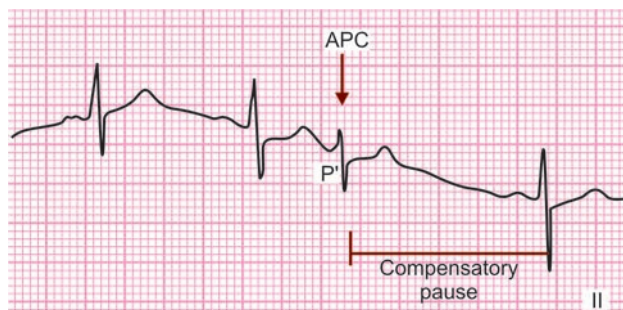
### ECG Characteristics (Fig. 5.23)

- A supraventricular (atrial or nodal) ectopic occurs prematurely so the P' wave is recorded earlier than the normal anticipated P wave.
- The abnormal P' wave of an ectopic may be upright, inverted or biphasic.
- The P-R interval of an ectopic beat may be short or absent (P is embedded within QRS).
- The premature impulse travels to the ventricles through normal pathway (bundle of His and ventricles), hence, the QRS complex is narrow and resembles normal sinus beat.
- The compensatory pause following each ectopic beat is usually incomplete ( $< 2$  R-R intervals).

## Paroxysmal Supraventricular Tachycardia (PSVT)

### Definition

Paroxysmal supraventricular tachycardia is defined as conduction of supraventricular impulses at a rate  $> 100$



**Fig. 5.23:** ECG strip showing a supraventricular (atrial) ectopic (a premature P' wave with short P-R interval and a narrow normal QRS)

bpm with narrow QRS, regular R-R intervals and without an evidence of pre-excitation. If it is associated with wider QRS, then it is called PSVT with aberrant conduction.

PSVT is a narrow QRS complex tachycardia at a rate of 150-250 bpm with sudden onset and sudden termination.

### Mechanisms

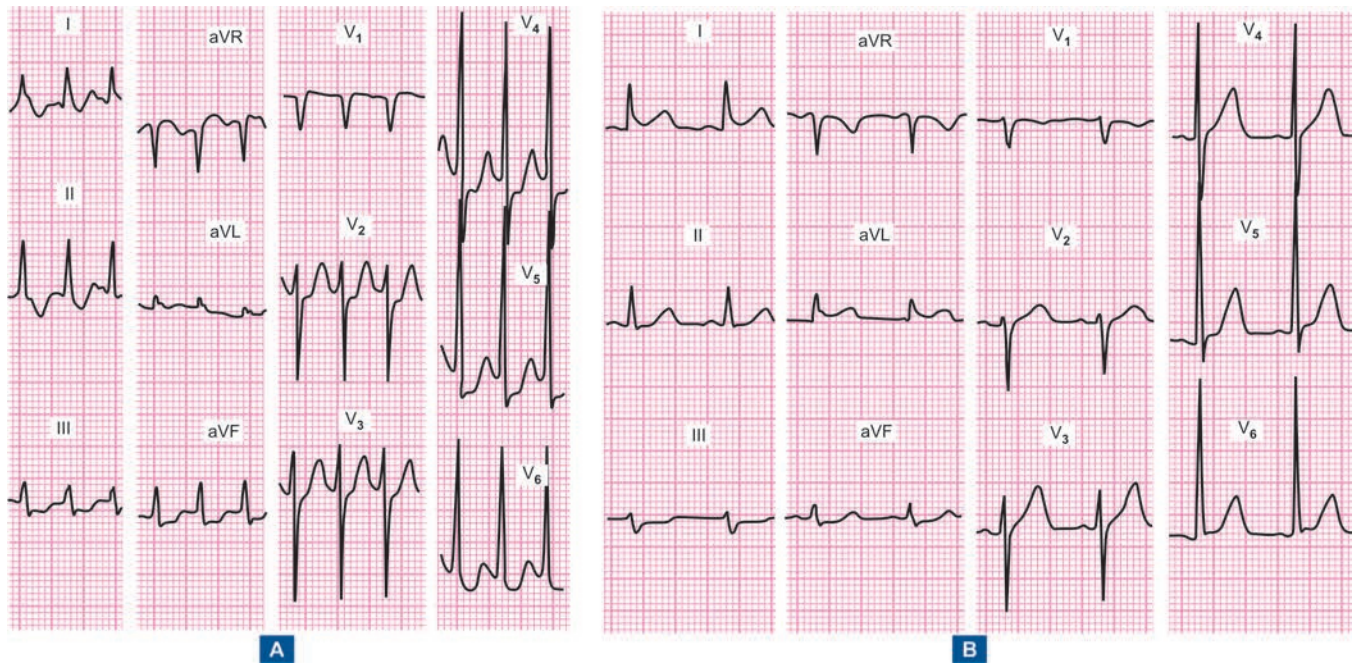
Re-entry is the basic mechanism which may occur at sinus, atrial or AV nodal level. AVNRT (AV nodal re-entrant tachycardia) is the commonest type.

- AV nodal re-entry
- AV nodal re-entry through a concealed extranodal pathway or atrioventricular re-entrant tachycardia (AVRT)
- SA node re-entry
- Intra-atrial re-entry
- It may be due to an excitation of an ectopic focus called *automatic atrial tachycardia*.

### ECG Characteristics (Figs 5.24A to C)

- The heart rate, e.g. atrial and ventricular is  $> 100$  bpm and regular (1:1 conduction).
- The P wave occurs simultaneously with QRS, hence, is not visible in AVNRT (AV nodal re-entrant tachycardia). However, in AV nodal re-entry with a concealed extranodal pathway (atrioventricular re-entrant tachycardia –AVRT), the 'P' wave follows QRS complex. In SA nodal re-entry or intra-atrial re-entry, the P wave precedes the QRS with a short P-R interval.
- The initiation and termination of the tachycardia is by an APC which has longer P-R interval in AVNRT while either shorter or normal P-R interval in AVRT (atrioventricular re-entrant tachycardia).
- The QRS complex is narrow and resembles normal QRS, hence, called narrow QRS complex tachycardia except in AVRT, where QRS complexes are wide.
- The nonparoxysmal SVT with second degree AV block is characteristic of digitalis toxicity rather than paroxysmal atrial tachycardia with block.





**Figs 5.24A and B:** Paroxysmal supraventricular tachycardia (PSVT)—a narrow complex tachycardia: A. ECG before reversion shows narrow complex tachycardia at a rate of 187/min (approx), regular, B. ECG after reversion shows normal sinus rhythm at a rate of 1500/16 = 93/min (approx) regular

**Table 5.6:** Differentiation between atrial flutter and atrial fibrillation on ECG

Feature	Atrial flutter	Atrial fibrillation
Atrial rate	Faster 350-400 bpm	Fastest 400-600 bpm
Ventricular rate	Regular. The R-R intervals are regular unless there is changing AV block. It is either the half or one-fourth of the atrial rate due to 2:1 or 4:1 block	Irregular as there is changing AV block. Irregular R-R interval differentiates it from atrial flutter where R-R is regular
P wave	The P wave are replaced by flutter (F) waves	P wave are replaced by fibrillatory (f) waves
Baseline	There is saw- tooth appearance of baseline	There is undulation of the baseline

### Treatment

See the algorithm (Fig. 5.24C).

### Atrial Flutter and Atrial Fibrillation

Both are supraventricular tachyarrhythmias characterised by rapid atrial rate, ineffective atrial contractions, replacement of P wave with either flutter (F) waves or fibrillation (f) waves and a rapid ventricular rate. The differences on ECG are summarised in Table 5.6.

Due to rapid ventricular rate and ineffective atrial contractions leading to reduced diastolic filling of ventricles, they can precipitate heart failure, angina and acute pulmonary oedema. They can predispose to

thrombus formation in the atrium leading to embolisation especially in atrial fibrillation (Figs 5.25 to 5.27).

### Causes

Causes of atrial fibrillation and atrial flutter are more or less some. They are given in Box 5.4.

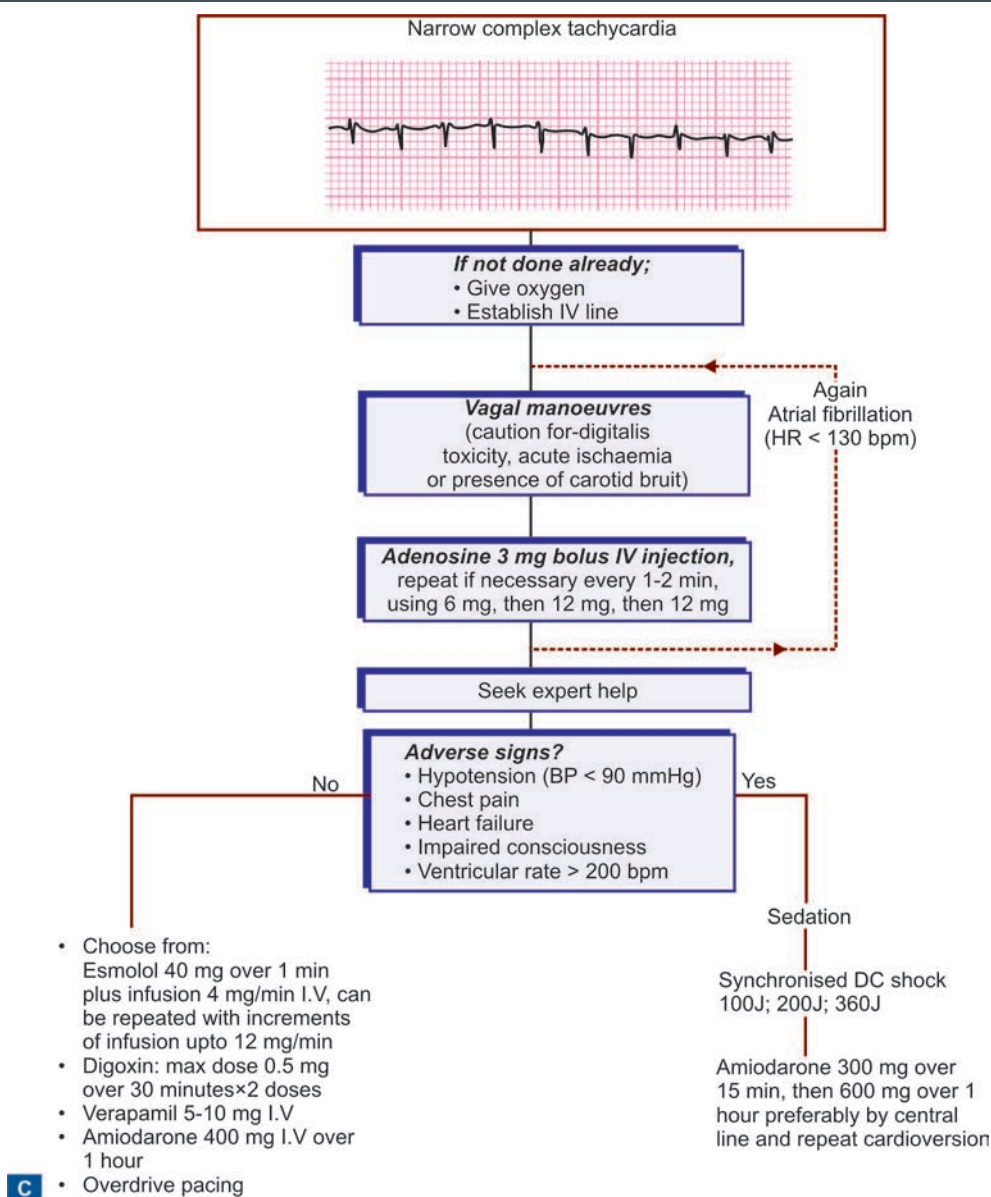
### The Electrocardiograms

Figure 5.25 shows atrial flutter with 4:1 conduction.

Figure 5.26 reveals fast atrial fibrillation while flutter fibrillation is depicted in Figure 5.27.

### Treatment

The aim of treatment is to convert atrial flutter and



**Fig. 5.24C:** Paroxysmal supraventricular tachycardia (PSVT)—a narrow complex tachycardia. Algorithm for treatment



**Fig. 5.25:** Atrial flutter, with 4:1 conduction. The ECG strip shows a “saw-tooth” appearance of the baseline due to replacement of normal P wave with flutter ‘F’ waves. Every 4th F wave is conducted and followed by a narrow QRS complex indicating 4:1 conduction. The R-R interval (heart rate) is regular



**Fig. 5.26:** Atrial fibrillation. The lead V<sub>1</sub> shows no visible P waves. The P waves have been replaced by “f” waves of fibrillation causing undulation of baseline. The R-R intervals are irregular indicating irregular ventricular response in atrial fibrillation. The QRS complexes are narrow and normal, hence, there is normal intraventricular conduction





**Fig. 5.27:** Flutter fibrillation. The rhythm strip shows wavy baseline due to large fibrillation waves resembling 'F' waves. The R-R intervals are irregular confirming it fibrillation rather than flutter, hence, called flutter fibrillation

**Box 5.4:** Causes of atrial fibrillation and atrial flutter

Common	Uncommon
<ul style="list-style-type: none"> <li>Rheumatic valvular heart disease</li> <li>Thyrotoxicosis</li> <li>Cardiomyopathies</li> <li>Coronary artery disease</li> <li>Myocarditis, e.g. diphtheria</li> <li>Hypertensive heart disease</li> <li>Mitral valve prolapse</li> </ul>	<ul style="list-style-type: none"> <li>Constrictive pericarditis</li> <li>Cor pulmonale</li> <li>Congenital heart disease, e.g. ASD, Ebstein anomaly</li> <li>WPW syndrome</li> <li>Left atrial myxoma</li> <li>Heart surgery</li> <li>Idiopathic (lone, atrial fibrillation)</li> </ul>

fibrillation to normal sinus rhythm as well as to slow the ventricular response. The steps of treatment are:

1. Correct the underlying cause; if unsuccessful then; slow the ventricular rate either by digoxin or a betablocker or a calcium channel blocker.
2. Add class IA (quinidine, procainamide, disopyramide) or class IC (flecainide) or class III (amiodarone) anti-arrhythmic to convert atrial flutter to normal sinus rhythm.
3. Synchronised DC shock (starting at 50 J), if patient is haemodynamically unstable.
4. Overdrive pacing may, at times, be used to convert atrial flutter to sinus rhythm.
5. Anticoagulants may be used to prevent thrombo-embolism especially in atrial fibrillation.

### Ventricular Arrhythmias

Arrhythmias originating from the ventricles are called *ventricular arrhythmias*. These include:

- *Ventricular ectopics or premature complexes (VPCs)* (Figs 5.28A to F). These may be monomorphic (same morphology) or polymorphic (different morphology), may be two in a row (ventricular couplet Fig. 5.28G), may exhibit R on T phenomenon (VPC falls on the T

wave of previous impulse) or may follow a bigeminy (an ectopic beat alternates with a sinus beat) or trigeminy (one ectopic falls regularly after two successive sinus beats) pattern.

- *Ventricular rhythm and accelerated ventricular rhythm.*
- *Ventricular tachycardia.*
- *Ventricular fibrillation and cardiac asystole.*

### Ventricular Ectopics

The ECG characteristics are:

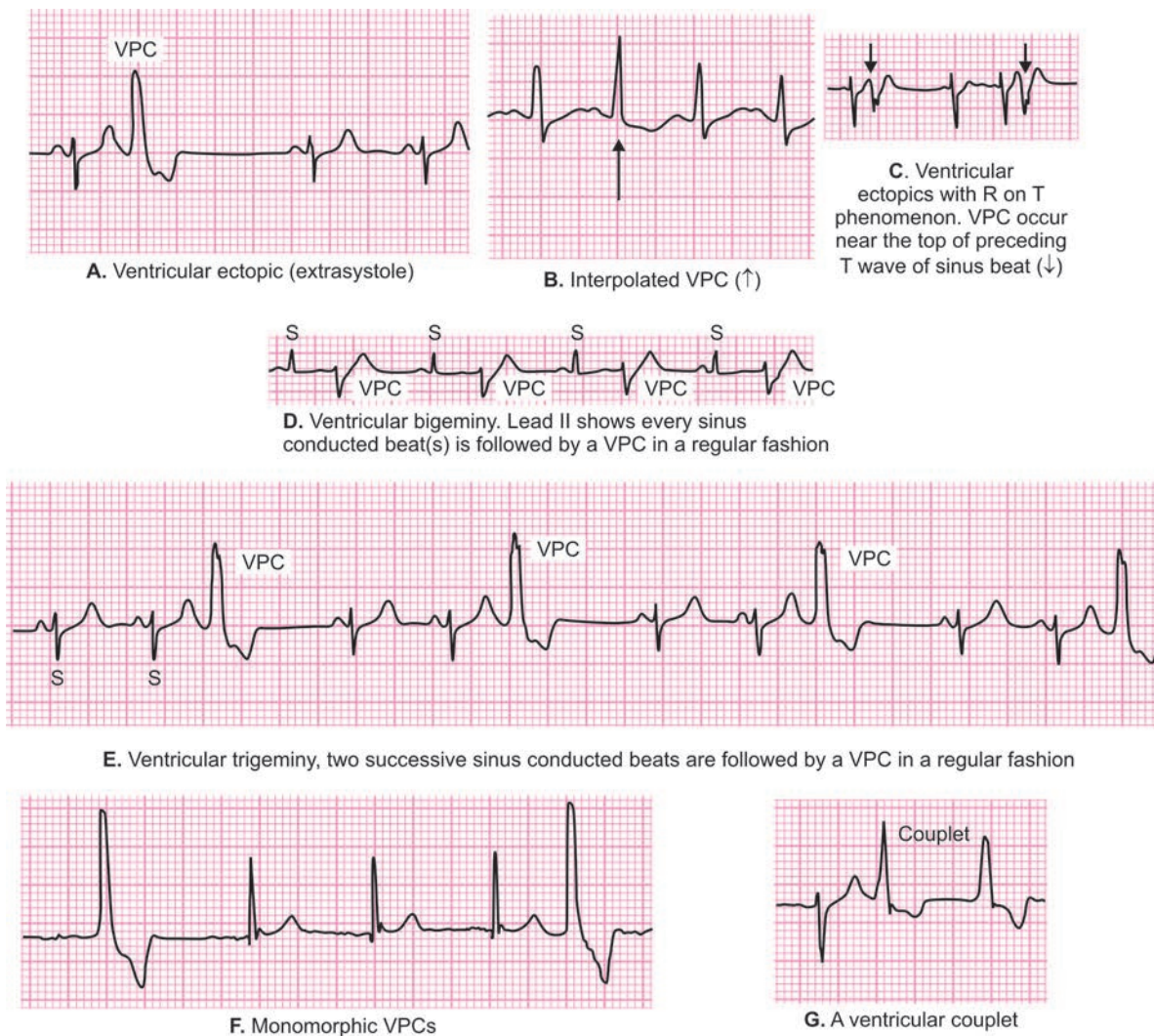
1. A VPC being premature occurs earlier than the expected sinus beat, hence, R-R interval becomes intermittently irregular.
2. The P wave of the ectopic beat is not visible. The P wave is embedded within QRS.
3. The QRS of the ectopic beat (s) is wide ( $> 0.14$  sec) and bizarre because a VPC originates from the ectopic focus and then spreads slowly and abnormally through the ventricles.
4. The pre-ectopic interval (interval between the VPC and preceding sinus beat) is shorter than post-ectopic interval (interval between the VPC and the following sinus beat).
5. A compensatory pause. A long interval that follows a VPC and ends with the next sinus beat is called *compensatory pause*. The compensatory pause is complete ( $2 \times$  R-R intervals).
6. The VPC shows ST segment depression and T wave inversion.

Causes of VPCs (Box 5.5)

### Ventricular Tachycardia (VT)

*Definition*

Ventricular tachycardia is defined as a series of 3 or more consecutive VPCs which are recorded in a rapid



Figs 5.28A to G: ECG showing VPCs

succession. It is either due to enhanced automaticity of a ventricular ectopic focus (rare) or due to re-entry within the ventricular myocardium (common).

**Causes** (Box 5.6)

**The ECG Characteristics** (Figs 5.29A to C)

1. The QRS complexes are wide ( $>0.14$  sec) and bizarre, hence, also called *wide QRS complex tachycardia*.
2. Ventricular rate is  $>100$  bpm.
3. The superior axis  $-140^\circ$  ( $-90^\circ$  to  $-180^\circ$ ).
4. Concordant pattern in precordial leads, i.e. all the complexes in precordial leads ( $V_1$ - $V_6$ ) are either downwards or upwards.
5. AV dissociation – a characteristic feature (Fig. 5.29C).
6. Presence of *fusion complexes* and *capture beats* within a run of VT (Fig. 5.29B).

**Capture beat (C)** is a normal sinus conducted beat (narrow QRS complex) within a run of VT.

**Fusion complex** is a complex produced by activation of the ventricles both by sinus and ectopic beats, hence, is a blend complex whose configuration is intermediate between the normal sinus beat and a ventricular ectopic.

**Differential Diagnosis of Wide QRS Tachycardia**

Wide QRS tachycardia may be due to:

- Ventricular tachycardia.



**Box 5.5: Causes of VPCs****Common**

- Physiological
- Stress, anxiety, excessive tea, coffee intake
- Coronary artery disease
- Acute MI
- Cardiomyopathies and myocarditis
- Valvular heart disease
- Digitalis-induced
- Hypertensive heart disease
- Electrolyte disturbances, e.g. hypokalaemia

**Uncommon**

- Alcohol intake
- Pericardial disease
- Cor pulmonale
- Following cardiac surgery or catheterisation
- Metabolic disorder
- Congenital heart disease
- Poisoning, bites, etc.

**Box 5.6: Causes of ventricular tachycardia (VT)**

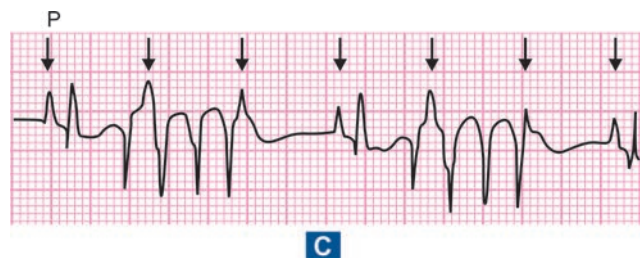
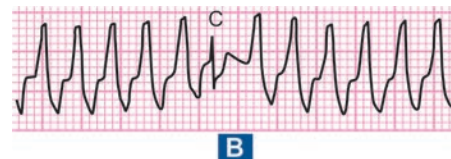
- Acute MI or myocardial ischaemia
- Cardiomyopathies
- Myocarditis
- Reperfusion
- Ventricular aneurysm
- Idiopathic arrhythmogenic right ventricular dysplasia
- Hypokalaemia
- Drug induced, e.g. digitalis
- Mechanically induced by a pacing catheter, pacemaker, etc.
- Idiopathic

- Supraventricular tachycardia with aberrant conduction.
- Bundle branch block tachycardia. Tachycardia in a patient with co-existing or pre-existing bundle branch block.
- Reciprocal tachycardia (tachycardia occurring in a patient with WPW syndrome, i.e. AVRT).

The two common types of wide QRS tachycardias are compared in Table 5.7.

**Treatment**

The treatment of wide QRS complex tachycardia is given in the algorithm (Fig. 5.30).



**Figs 5.29A to C: Ventricular tachycardia (VT):** A. Nonsustained VT. The leads II, III and aVF shows a ventricular triplet, B. ECG strip shows a run of VT with a capture beat (c), C. Ventricular tachycardia showing AV dissociation

**Table 5.7:** Differentiating wide QRS tachycardia

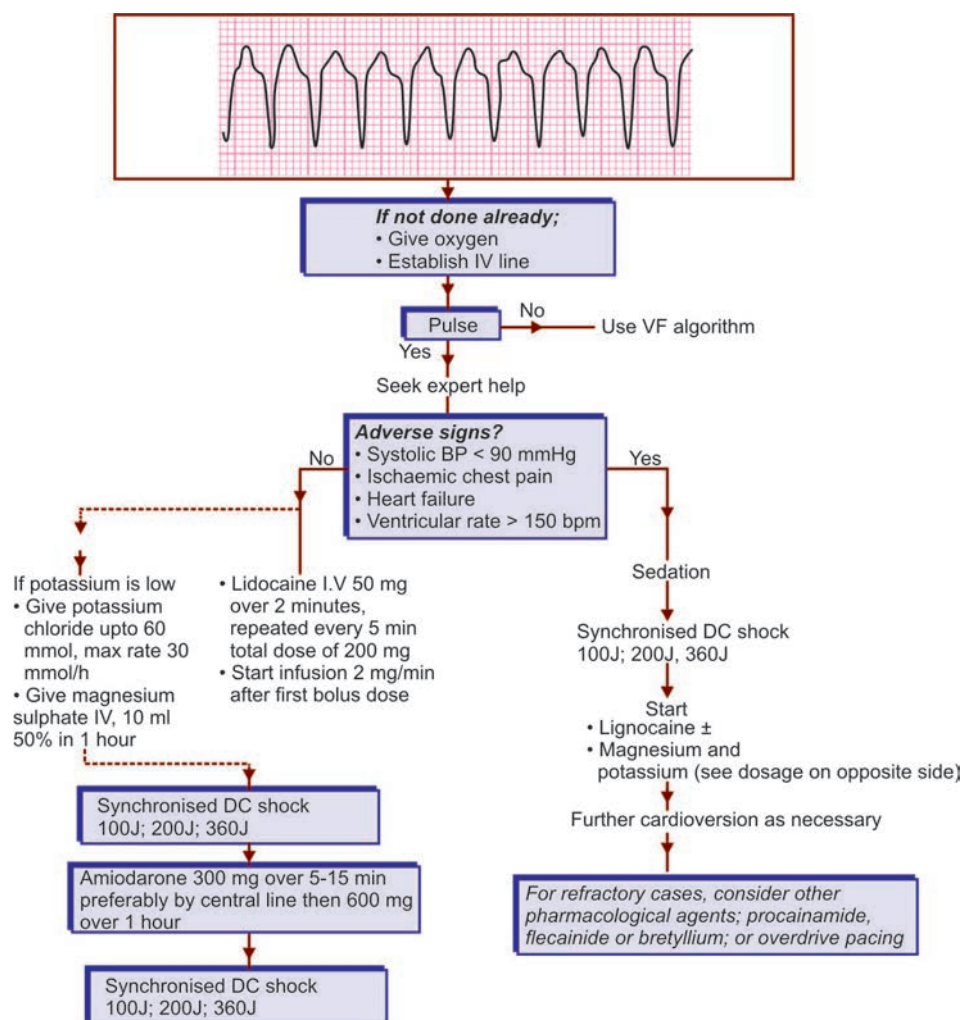
Feature	Supraventricular tachycardia (SVT) with aberration	Ventricular tachycardia (VT)
P wave	A premature P may precede QRS	Not preceded by P wave
QRS morphology	RSR' in V <sub>1</sub> and RS with wide S in V <sub>6</sub>	Slurred R, RR' or QR in V <sub>1</sub> or rS or qR in V <sub>6</sub>
QRS duration	<0.14 sec	>0.14 sec
R-R interval	Regular	Irregular, can be regular
Axis	Right or left	Superior
AV dissociation	Not seen	Seen
Fusion and capture beats	Absent	Present – a diagnostic feature

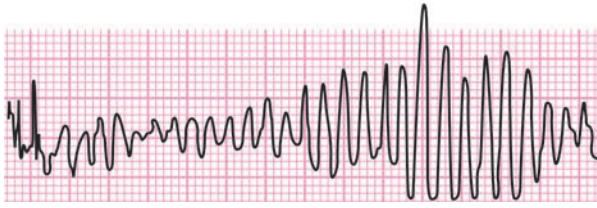
### Torsades de Pointes

It is a polymorphic ventricular tachycardia in which the QRS complexes of varying amplitudes appear to twist around a isoelectric baseline, hence, its name. It is characteristically seen after prolonged QT interval. It is often self-limiting but can degenerate into ventricular fibrillation, hence, also called multifocal ventricular flutter.

#### Causes

- Class I antiarrhythmics.
- Hypokalaemia, hypocalcaemia and hypomagnesaemia.
- Psychotropic drugs (e.g. phenothiazines, antidepressants, antihistaminics, pentamidine and some antimalarials).

**Fig. 5.30:** Algorithm for treatment of broad QRS complex tachycardia



**Fig. 5.31:** Torsades de pointes. The ECG strip was recorded from a patient with long Q-T syndrome. The rhythm strip recording during palpitation shows polymorphic ventricular tachycardia in which wide QRS complexes of varying amplitude are twisting around the baseline

- Acute myocardial infarction, mitral valve prolapse, myocarditis, Prinzmetal's angina.
- Weight reducing liquid protein diets and starvation.
- Congenital prolonged Q-T syndrome.
- Acquired prolongation of QT due to any cause.
- CNS lesions, e.g. subarachnoid haemorrhage.

#### ECG Characteristics (Fig. 5.31)

- It is usually initiated by a VPC with prolonged QTc interval or a VPC with R on T phenomenon.
- The polarity of QRS complexes alternate around the isoelectric baseline. The QRS complexes are wide, bizarre and their axis undulates for a short period leading to complexes which are directed upwards for a short period and then get directed downwards.
- The ventricular rate is rapid (200-250 bpm).
- The amplitude of QRS may show waxing and waning.

### Ventricular Fibrillation and Ventricular Asystole

Ventricular fibrillation is a catastrophic dysarrhythmia characterised by disorganised or chaotic electrical activity of the heart, which results in irregular and deformed QRS complexes of varying heights, widths and shapes. In the absence of ECG monitoring, it is difficult to distinguish it from ventricular asystole. The condition is terminal, unless cardioverted.

#### Causes

- Coronary artery disease
- Drugs, e.g. digitalis, adrenaline, anaesthetics
- Cardiomyopathy
- Electrolyte imbalance

- During cardiac surgery
- Hypothermia
- Accidental electric shock
- Failure to synchronise DC shock.

#### ECG Characteristics

- There are no identifiable waveforms. There is an undulating wavy baseline due to bizarre complexes that vary in size and shape.

#### Treatment

See the algorithm (Fig. 5.32)

### Ventricular Asystole

Ventricular asystole is defined as complete absence of electrical activity of the heart. Asystole, also called *cardiac standstill*, represents a terminal cardiac event (dyeing heart) and cannot be distinguished from ventricular fibrillation without ECG monitoring.

#### Causes

- Protracted episodes of VF
- Failure of pacemaker activity of the heart due to any cause such as drugs, acute MI and so forth.
- A terminal event in all acute catastrophic cardiovascular conditions.

#### The ECG Characteristics (Fig. 5.33)

- No ECG waveforms are identifiable
- The baseline appears wavy or flat as a straight line.

#### Treatment

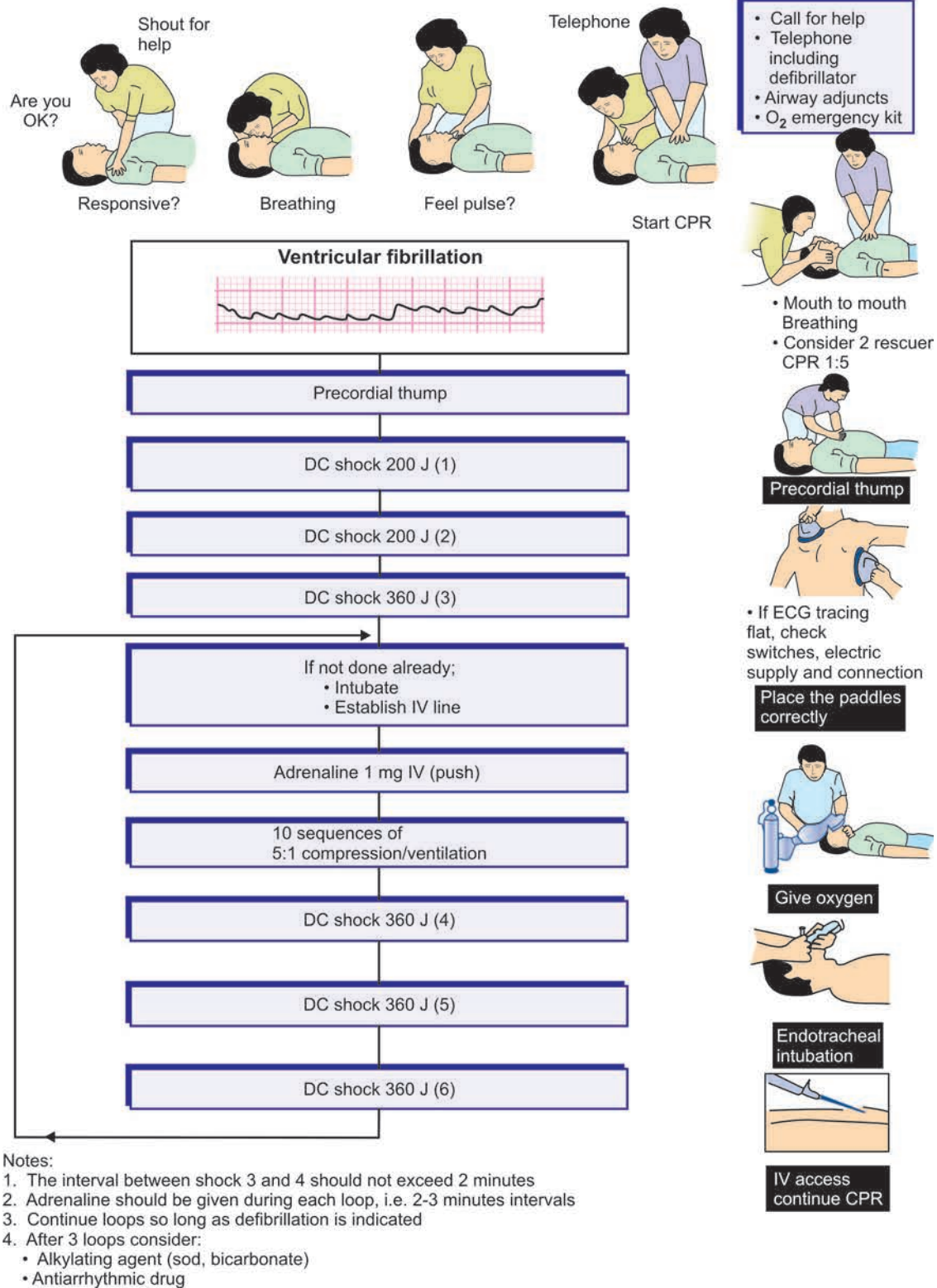
(See the algorithm Fig. 5.34)

## CONDUCTION DEFECTS

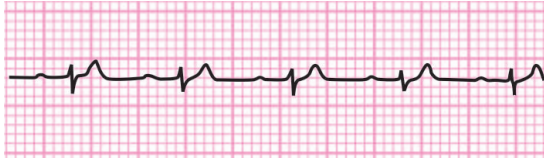
### Heart Blocks (AV blocks)

AV blocks represent either delay in conduction through AV node which prolongs the P-R interval; or cause intermittent or absent conduction between atria and the ventricles (absent QRS complex with production of a pause).





**Fig. 5.32:** Algorithm for managing ventricular fibrillation and pulseless ventricular tachycardia



**Fig. 5.33:** Ventricular asystole

### First Degree AV Block

There is delay in conduction of sinus impulse through AV node resulting in prolongation of P-R interval beyond upper limit of the normal, i.e. 0.20 sec.

#### ECG Characteristics (Fig. 5.35)

- The rhythm is regular, P-P and R-R intervals are constant
- Each P wave is followed by QRS, hence, there is no dropped beat
- The P-R interval is consistently prolonged beyond 0.20 seconds at normal heart rate and 0.22 sec. at heart rate of 60/min
- The QRS complexes are narrow and normal.

#### Causes

- Vagotonaemia
- Drugs (digoxin, betablockers, calcium channel blockers)
- Coronary artery disease
- Myocarditis
- Degeneration of conducting pathways associated with ageing
- Acute rheumatic carditis
- Congenital heart disease (ASD, Ebstein's disease)
- Hyperkalaemia
- Idiopathic

#### Treatment

Treat the underlying cause.

### Second Degree AV Block

There is intermittent interruption of AV conduction with the result some of the sinus or atrial impulses (P waves) are conducted to the ventricles while others are blocked

(blocked P or P wave not followed by QRS) producing a pause.

Causes (Box 5.7)

#### Box 5.7: Causes of second degree AV block

- Physiological e.g. athlete, vagotonic individual
- Diphtheric myocarditis
- Myocardial infarction or ischaemia (inferior wall, right ventricular)
- Drugs – digitalis
- Infiltrative heart disease, e.g. amyloidosis
- Acute rheumatic carditis
- Aortic valve disease
- As a protective mechanism with fast ventricular rhythms, e.g. atrial tachycardia, atrial flutter
- Idiopathic fibrosis of conducting system
- Calcification of mitral or aortic or both valves

#### Types

Second degree AV block is of two types:

##### Mobitz type I (Wenckebach type)

In this type, there is progressive prolongation of P-R intervals till one beat is dropped or blocked, i.e. that P is not followed by QRS. The resulting pause allows the conduction system to recover and the cycle is repeated again. Therefore, in this type, there is group or cyclic beating in which few beats show successive increase in P-R intervals and then one P is blocked. This period of group beating is called *Wenckebach period*. For example, in a group beating of 6 beats (P waves) the conduction sequence will be 6:5 second degree AV block (Fig. 5.36).

#### ECG Characteristics:

- The basic rhythm is sinus. The P-P intervals are constant.
- The P-R interval of successive beats lengthens in a cyclic manner (group beating is present) until one P is blocked.
- The conduction ratio varies, e.g. 6:5, 5:4, 4:3, etc.

##### Mobitz Type II AV Block

In this type, certain sinus beats are conducted and some are blocked in a variable or fixed manner (constant block).

#### ECG Characteristics (Fig. 5.37)

- P-R interval of conducted beats is constant and fixed

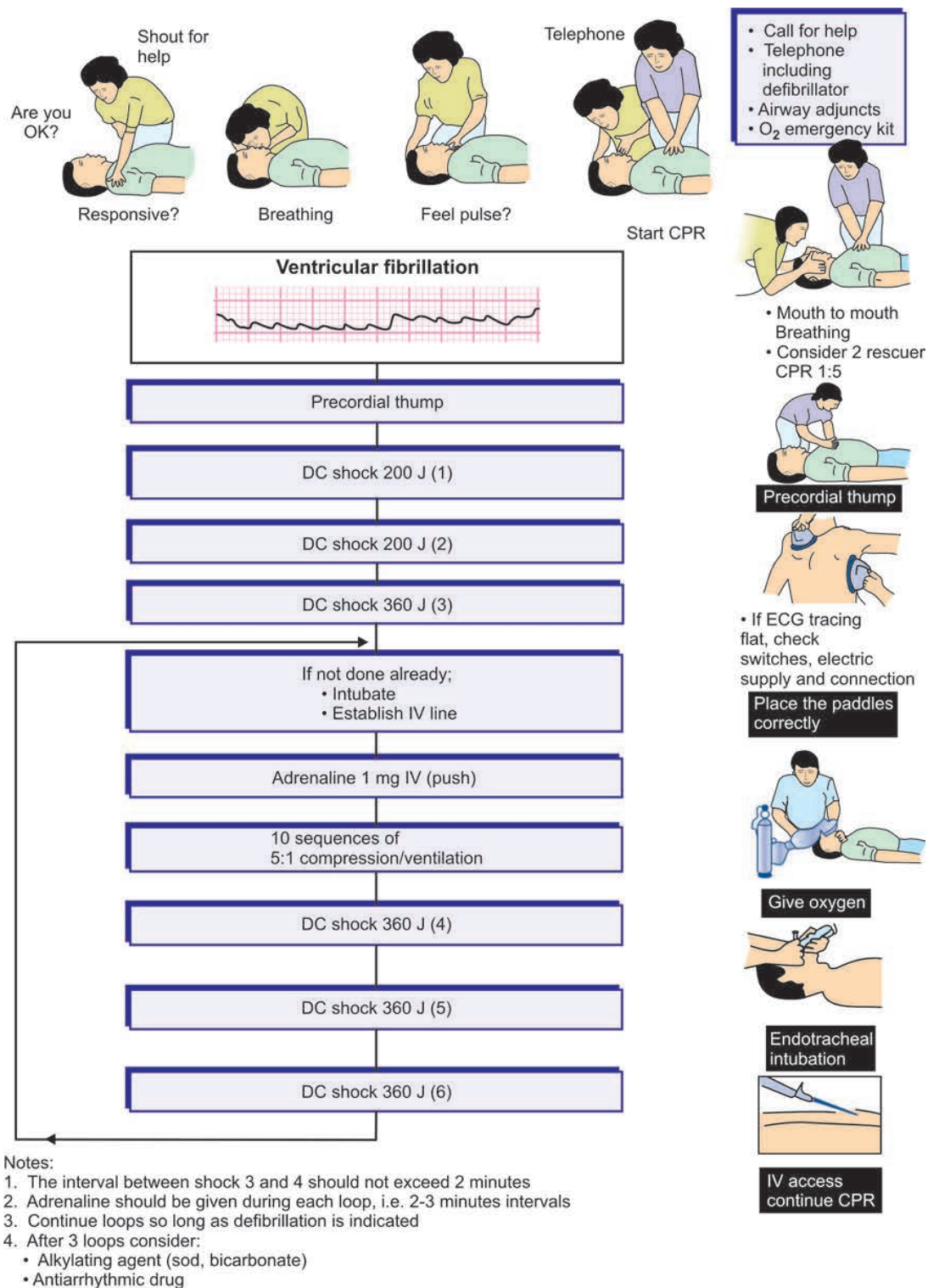
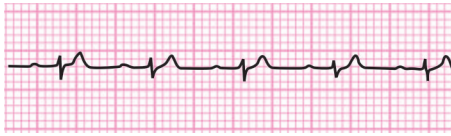


Fig. 5.34: Algorithm for asystolic cardiac arrest





**Fig. 5.35:** First degree AV block. Note the prolonged P-R interval i.e. 0.32 sec

- P-P intervals are constant and regular
- The R-R intervals are irregular due to dropping of some beats producing intermittent pauses
- The conduction sequence (the ratio of total beats to the conducted beats in a sequence in which P waves are counted after the dropping of the beat and includes next nonconducted P wave) may be fixed 3:2, 2:1 or variable.

### Complete (third degree) AV Block

This is characterised by complete interruption of AV conduction between the atria and ventricles resulting in dual rhythm, i.e. two independent pacemakers- one in the sinus node or atria and other in the ventricle are maintaining the cardiac rhythm, therefore the resulting rhythm is called *ventricular escape rhythm* which means ventricles have escaped from the control of sinus node and maintain their own rhythm.

These two rhythms beat asynchronously and at different rates, hence, the P waves and QRS complexes

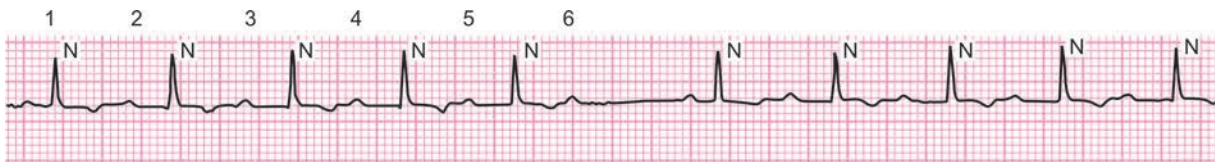
occur regularly but they do not bear any constant relationship. The rate of QRS (ventricular rate) is lower than P wave (atrial rate).

### Causes

- Congenital AV block
- Acute MI (inferior wall, right ventricular). It is transient in MI
- Hypervagotonaemia
- Acute rheumatic carditis
- Congenital heart disease (VSD, ASD-ostium primum)
- Lenegre's idiopathic degeneration and fibrosis of conduction system
- Lev's disease
- Myocarditis, pericarditis, Chagas' disease
- Cardiac surgery
- Infiltrative heart disease (amyloid, myxomatous)
- Space occupying lesion near the AV node (e.g. tuberculoma, gumma)

### ECG Characteristics (Fig. 5.38)

- The P-P and R-R intervals are constant
- The atrial and ventricular rates are different. The atrial rates are faster than ventricular, hence, there are more P waves than QRS complexes.



**Fig. 5.36:** Second degree Mobitz type I (Wenckebach) AV block. There is cyclic beating in which 6 beats are taking part. The P-R interval of each successive beat is prolonged from first to 5th while 6th P is blocked, hence, it is 6:5 Mobitz type I second degree AV block. After dropping the P wave, the cycle is again repeated



**Fig. 5.37:** Second degree Mobitz type II AV block. There is fixed 2:1 AV block (one P wave is dropped and second is conducted regularly)



**Fig. 5.38:** Complete heart block. The P-P and R-R intervals are constant. There is no relation of P wave to QRS indicating two independent pacemakers; one in the atrium or SA node and second below the AV node (e.g. in ventricle). The QRS is wide and bizarre indicating ventricular escape rhythm at a rate of 50/min. The atrial rate is 120/min, regular

- There is no relation of P wave to QRS, i.e. there is complete dissociation between P waves and QRS complexes.

- The configuration of QRS varies from narrow to wide depending on the site of ventricular pacemaker.
- The basic rhythm is either sinus or one of the supraventricular, e.g. atrial tachycardia, atrial flutter, atrial fibrillation.

#### *Treatment*

- Withhold the possible causative drug or treat the underlying cause
- Atropine can be given to accelerate the sinus rate
- Administer epinephrine for short-term ventricular support
- Insertion of temporary or permanent pacemaker depending on the cause.



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